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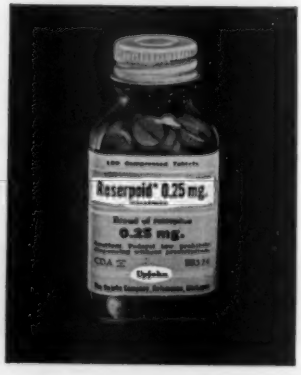

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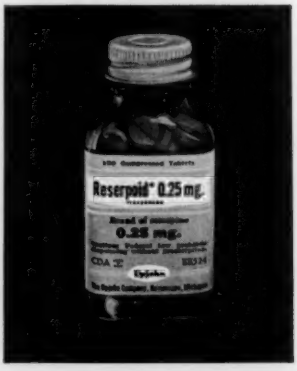

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1. Greenstein, L., and Sapirstein, M. R.: A. M. A. Arch. Neurol. & Psychiat. *70*:469 (Oct.) 1953. • 2. Smith, B., and Forster, F. M.: Neurology *4*:137 (Feb.) 1954. • 3. Smith, B. H., and McNaughton, F. L.: Canad. M. A. J. *68*:464 (May) 1953. • 4. Whitty, C. W. M.: Brit. M. J. *2*:540 (Sept. 5) 1953. • 5. Doyle, P. J., and Livingston, S.: J. Pediat. *43*:413 (Oct.) 1953. • 6. Timberlake, W. H., Abbott, J. A., and Schwab, R. S.: New England J. Med. *252*:304 (Feb. 24) 1955.

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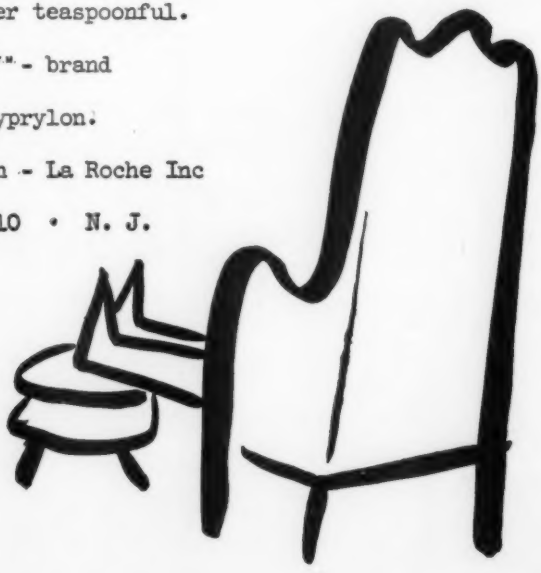

Volume 5 Neurology *Number 6*

Syndrome of Klüver and Bucy

Reproduced in Man by Bilateral Removal of the Temporal Lobes

Hrayr Terzian, M.D. and Giuseppe Dalle Ore, M.D.

In 1937 Klüver and Bucy[1] described some behavior changes which represent "the most striking behavior changes ever produced in animals" as a result of bilateral operative removal of the temporal lobes, including most of the uncus and hippocampus in the Macacus rhesus. These behavior changes consisted of 1) "psychic blindness" or "visual agnosia;" 2) strong oral tendencies; 3) the so-called "hypermetamorphosis" or excessive tendency to attend and react to every visual stimulus; 4) considerable changes in emotional behavior characterized by a remarkable decrease of aggressive behavior and by loss of fear reactions; 5) an increased sexual activity involving forms of heterosexual, homosexual, and autosexual behavior; and 6) considerable changes in dietary habits.[2–5] In Klüver and Bucy's experimental work this syndrome was not produced by lesions of other lobes, or by unilateral temporal lesions, or by removal only of the lateral temporal cortex both unilateral or bilateral. The experimental work of Klüver and Bucy was supported more recently by Thomson and Walker[6] who studied the effects of minor rhinencephalic removals in the Macacus rhesus, by Bard[7] in the same animal, and by Gastaut[8] and Schreiner and Kling[9] in cats.

Bard and Mountcastle[10] had, on the other hand, demonstrated that bilateral removal of practically the same rhinencephalic structures in cats produces savageness and a considerable increase of rage reactions. Bard and Mountcastle, who succeeded in converting a placid state produced in cats by neocortical removal to one of ferocity by removal of "pyriform lobe, amygdala, and hippocampus," put forth the hypothesis that the amygdala "acts as a funnel through which inhibitory influences originating

From Clinica delle Malattie Nervose e Mentali dell'Università di Padova and Reparto Neurochirurgico dell'Ospedale Civile di Padova, Italy.

Read at the Fourth Italian Neurosurgical Congress, Rapallo, December 1953.

in the transitional cortex of the midline, in the neocortex, and in the amygdala itself, exert a suppressing action on brainstem mechanisms" involved in rage reactions. The differences between the results of Bard and Mountcastle and those of Klüver and Bucy were considered to be due to differences of species of animals used in the two groups of experiments. But the recent experimental studies of Gastaut and of Schreiner and Kling, though demonstrating the differences due to the animal species, suggest the hypothesis that in the two groups of experiments the removed structures were not completely analogous.

More or less complete unilateral surgical removal of the temporal lobes in man (including most of uncus and hippocampus), as surgical treatment of psychomotor epilepsy, did not produce evident changes of behavior and psychic functions.[11,12] As a matter of fact, the unilateral amputation of the temporal lobe with removal of the uncus and hippocampus is today proposed as the most rational surgical therapy of temporal lobe epilepsy.[11–16]

More or less complete bilateral removal of the temporal lobes has been recently practiced in man also, both for the purpose of removing bilateral epileptogenic foci and, directly inspired in this by the experimental work of Klüver and Bucy, for the purpose of modifying aggressive behavior and agitation in schizophrenic subjects. These operations have not yet been published in detail. In a few cases, however, we came to know of some isolated elements of the Klüver and Bucy syndrome, such as hypersexuality, bulimia, and more or less severe memory defects.[14,17–23]

We think it useful to report here a human case in which the complete syndrome occurred as the result of bilateral temporal lobectomy, including most of the uncus and hippocampus.

A 19 year old boy was admitted to the hospital on August 26, 1952 with a history of seizures. The patient was born at full term and developed normally. He attended up to the last grade of the elementary school with satisfactory results. In early childhood he was subject to spasms associated with loss of consciousness. When three years old he was afflicted by an attack of fever lasting seven days. Some months later he began to suffer from epileptic attacks of psychomotor and grand mal type, with rotation of the head and eyes to the right, and they were followed by paresis of the right extremities. Almost all these attacks were preceded by terrifying visual hallucinations, rarely by auditory hallucinations. Fits of minor scale were followed by long states of confusion with various automatisms from the most simple to the most complex. In addition to this the patient presented considerable changes of character, which became more accentuated in the following years and were accompanied by paroxysms of aggressive and violent behavior. Several times during these attacks, he attempted to strangle his mother or to crush his younger brother under his feet. The brother had a history of nocturnal enuresis and presented an epileptic type of electroencephalogram.

When admitted to the hospital on August 26, he presented only slight signs of right hemiparesis. Radiologic examinations and laboratory tests were negative. During his stay in the hospital the patient had several attacks, many times a day, some followed (rarely preceded) by long confusional states during which he attacked the nurses and tried to commit suicide. In spite of these severe attacks the patient enjoyed periods of mental lucidity lasting one or two weeks, in which he revealed a well-preserved memory, a serviceable character, and normal intelligence (Wechsler-Bellevue, normal average). The electroencephalogram showed a considerable amount of diffuse normal alteration and an important epileptogenic focus in the left temporal region with signs of an independent contralateral temporal focus. Since the attacks persisted in spite of all medical therapy, the patient underwent

surgery on October 12, 1952 on the basis of electroencephalographic localization. The entire anterior portion of the left temporal lobe as far as the vein of Labbé (7 cm. on the base line and 5 cm. on the fissure of Sylvius) and medially most of the uncus and hippocampus were removed. The postoperative course was quite satisfactory. A right hemiparesis developed as well as some traces of aphasia which disappeared within a few days. Some days later the attacks reappeared. During his psychomotor episodes the patient attacked the nurses and doctors and threatened some doctors with death. No real improvement was noticed in his behavior or psychic condition. Nineteen days after the first operation, the right temporal lobe was removed according to the topographic limits mentioned above, for the purpose of modifying at least his violent and aggressive behavior. This was done on the basis of favorable results obtained by Paillas[18] in two similar cases. No motor or sensory defects and in particular no hemianopia followed this second operation, but a complex syndrome quite similar to that described by Klüver and Bucy appeared.

The syndrome, as Klüver and Bucy had noticed in their monkeys, was observed soon after operation and from then on varied only in very slight degree. In order to follow their scheme, we shall give a brief description of the patient's outstanding symptoms instead of a chronologic exposition. It was impossible to make an accurate and detailed analysis of this subject's psychic symptomatology because of the syndrome itself, as will appear clearly from the following description.

1. The first evident phenomenon noticed in the patient soon after the operation was the fact that he did not recognize anyone, including his closest relatives. During the first month after the operation, he treated his mother in exactly the same manner as he did the nurses, calling her "Madam." This was most surprising in view of the fact that the patient was deeply attached to his mother, toward whom he had previously demonstrated, in his periods of lucidity, an affection his mother herself considered exaggerated. In the following months he called his parents "mother and father" but manifested no particular affection for them. He distinguished the doctors with whom he was daily in contact only by some somatic characteristics which attracted his sexual interest (see later on).

2. During the first week after operation the patient presented a considerable reduction of spontaneous motor activity, which caused him to remain in bed or to sit for a long time in an almost catatonic attitude. In this period it was impossible to communicate with him and his attention could not be attracted even by shouting very close to his ears. After about 15 days, however, he showed a strong tendency to approach all people who passed near him and to take possession of all objects surrounding him. Klüver, following Wernicke, calls this tendency "hypermetamorphosis" or "hypermetamorphic impulses to action." The patient would stop anyone he met, addressing to them all the same four or five elementary questions. In this second period it was difficult to draw his attention even by shouting at him; it was much easier to attract his attention by repeating one of his customary gestures. For instance, the characteristic gesture of stroking one's mustache became in a few days the conventional signal to start a conversation with the patient. But this contact never lasted longer than a few minutes since the patient was easily distracted. One was obliged to repeat the conventional signal in order to resume the interrupted conversation which invariably concerned his meals, his return home, and his sexual problems.

In addition, the patient showed a remarkable tendency to imitate the manners of the surrounding people (doctors, nurses) and would even reproduce professional gestures. For instance, he examined x-ray plates, raising them against the light, or tried to prepare an injection syringe.

The oral tendencies described by Klüver and Bucy in the monkey did not appear in this patient. He picked up objects, limiting his interest to a superficial inspection of them, passing from one to another, picking up the same object again and again, without showing particular concern for any single one.

3. Some days after the operation the patient demonstrated an insatiable appetite and ate at least as much as four normal persons. He prepared himself for meals as for a ceremony. He would personally go to the kitchen and insistently ask for food at any hour. He would look for a secluded corner far from anyone, eat everything voraciously without preference for any certain food, lick the dish incessantly, and after 15 minutes asked for more food.

4. The patient's speech remained practically unaltered as far as elaboration and pronunciation are concerned. There were no signs of aphasia of any kind. His language, on the contrary, had become poorer and was composed of very elementary sentences within the limits of his natural needs, concerning the present and without reference to the past. He continuously repeated these very few sentences with exasperating perseverance and would not permit himself to be interrupted.

In the reading tests a partial alexia became evident. He could read and pronounce letter by letter, but he was not able to distinguish one word from another. In short, he did not distinguish the meaning of the words he had just read. Only some words, such as "Verona" (his birthplace), "mother" and "father" were recognized by him, and after long delay provoked a corresponding question, such as "when will mother come?" or the remark, "I live in Verona."

When asked to write whatever he wanted to he would write only his Christian and family names, but very slowly, stopping at each letter. He did not write anything spontaneously, although before the operation he kept a diary. He succeeded in writing a few words to dictation but very, very slowly and soon becoming tired. He could not write more difficult words.

His chronologic sense of time was rather well preserved. He could distinguish yesterday from today and from tomorrow. In speaking he used the correct verbal construction but mispronounced similar words easily, sometimes inverting the order of syllables and creating, by assonance, new terms. In some sentences he skipped words (for example, "the bearded watch" instead of "the watch of the bearded doctor").

5. Fifteen days after the operation the patient's attention was attracted by the sexual organs of an anatomic scheme hanging on the wall of the examining room. On that occasion he displayed to the doctor, with satisfaction, that he had spontaneous erections followed by masturbation and orgasm. From then on the patient gradually became exhibitionistic. He wanted to show his sexual organ erect to all doctors. He never manifested any sexual aggressiveness toward persons of the female sex for whom, on the contrary, he showed indifference in contrast with his behavior before the operation. Homosexual tendencies, clearly expressed by verbal invitations to some doctors, were soon noticed. Although monotonously insistent, he did not manifest the slightest aggressiveness either verbally or with gestures. At present, about two years after the operation, the patient is now in a mental hospital, practices self-abuse several times a day, but shows no aggressiveness either toward the male or female sex. The homosexual tendency still persists.

6. The most evident and surprising phenomenon for the observer was the complete loss of any emotional behavior in the patient. He no longer manifested the slightest rage reactions toward the nurses and doctors, upon whom, before the second operation, he used to rush as soon as they came into sight. The patient, on the contrary, now assumed an extremely childish and meek behavior with everyone and was absolutely resistant to any attempt to arouse aggressiveness and violent reactions in him. He was completely indifferent toward everyone, including his parents; his relations with relatives, the doctors and nurses were limited to those conventional questions he addressed to everyone with tedious insistence, questions concerning meals and his return home. He attached no importance to any reply.

In addition, the patient manifested complete amimia, sometimes replaced by a conventional and unmotivated smile. An emotional expression was noticed in the patient's face only once when he saw his image in a mirror, betraying a childish satisfaction because he had found human features in a lifeless object. From then on he liked to look at himself for many hours in the mirror.

His voice became monotonous and deprived of any emotional coloring, while its tone changed altogether, becoming lower.

7. There was a serious disorder in his memory. Not only did he not remember at all what had recently happened, he did not remember anything of his past. Even when we insisted on knowing something about his house, his family, the city he lived in, the patient did not even seem to understand these questions, as if their object was entirely unknown to him. It was not possible to analyze his memory functions, but we can affirm that the patient felt completely isolated, without a past to remember and consequently without any future whatever.

8. His orientation in space was altered. He

did not realize in which city or place he was and he expressed himself as if his native town (Verona) was situated close by, although he walked around the place where he was now living without making mistakes, such as opening the wrong door or going to the wrong bed.

9. The patient became very orderly and meticulous in his habits, very jealous of his belongings which he wanted to keep nearby, specifying for every object, "this is mine, this is mine." He always kept himself clean.

10. The first days after the second operation a certain drowsiness was noticed. After about ten days the patient had recovered his normal sleep-waking rhythm. The arterial pressure was the same as before the operation and the other vegetative functions remained unaltered. No remarkable modifications were noticed in the biologic constants.

The generalized epileptic attacks, which had disappeared in the first two months after the operation, reappeared later on with the same motor characteristics (grand mal) and with the same frequency as before the operation. He never again presented psychomotor attacks.

DISCUSSION

The detailed analysis we have made of this complex syndrome has obviously a merely descriptive purpose. All the various elements we isolated artificially formed a single whole in which the change of emotional behavior acquired predominant importance.

First of all, this case must undoubtedly be considered as a dramatic confirmation of the experimental studies of Klüver and Bucy. It reproduces all the symptomatology brought into evidence by these authors in monkeys, except for the oral tendencies. Most likely these tendencies, together with other slighter differences, are closely associated with the animal species.

From the point of view of the anatomic correspondence of the surgically removed structures (although it is difficult to determine from the surgical report), we can say that the following structures were removed bilaterally: the anterior portion of the temporal lobes in front of the vein of Labbé, the uncus, the anterior part of the hippocampus, and the amygdaloid nucleus. It is absolutely impossible to ascertain from a single case which structures are the most directly concerned in determining this complex syndrome. The results of Klüver and Bucy and the more recent ones obtained by Thomson and Walker[6] give more importance to the hippocampus, uncus, amygdaloid nucleus, and to the medial surface of the temporal lobe rather than the lateral temporal cortex.

It is evident, on the other hand, as Klüver and Bucy have already pointed out, that the syndrome provoked by this operation gives support to Papez's brilliant theory of the anatomophysiologic mechanisms of emotion. Papez[24] expressed the hypothesis that the so-called rhinencephalic structures, far from representing olfactory centers as the classical anatomophysiologic literature maintained, could be considered one of the fundamental elements of the circuit formed by the hypothalamus, the anterior thalamic nuclei, the gyrus cinguli, the hippocampus, and their interconnections which constitute a mechanism elaborating "the functions of central emotion" and participating in "emotional expression." Papez's hypothesis, on the other hand, is proved by the whole recent clinical and experimental literature on temporal lobe epilepsy. In this particular epileptic syndrome, convulsive activity originating in the structures of the temporal region and particularly in the rhinencephalon manifests itself through modification of the subject's behavior, particularly through modification of his emotional behavior.[25]

Klüver and Bucy[3,4] asked themselves

whether the complex syndrome they had produced by removing bilaterally the temporal lobes (including part of the rhinencephalon) might be interpreted as the expression of a disturbance in some one vital fundamental and elementary mechanism. They did not think they could give a precise answer to such a question, although they attached a greater importance on one side to "psychic blindness" (or "visual agnosia") and on the other side to "hypermetamorphosis" understood as a loss of Von Monakow's ekklisis. They concluded that "the symptoms involved heterogenous mechanisms which happen to be thrown into action at the same time when certain anatomical structures and their connections are damaged or eliminated." [4]

Although it is very difficult and rather risky to judge by one single case, without excluding the hypothesis of a disturbance of several mechanisms, we think that the greatest importance should be attributed to the impressive changes of emotional behavior. Two years after the operation the patient had lost the capacity to experience any emotion or to express it; he remained excluded from emotional contacts with other human beings, particularly with his own parents. He addressed his parents "sir" and "madam" and later "father" and "mother," but he did not recognize them in their emotional significance. He behaved in the same manner with everyone with whom he had been either on friendly or hostile terms during his long preoperative stay in the hospital. He no longer recognized persons in their emotive value. The same may be said of objects and symbols which became emotionally indifferent to him. However, he did not present "visual agnosia," by which term Klüver and Bucy described in monkeys the loss of "ability to recognize and detect the meaning of objects on the basis of visual criteria alone," since visual agnosia in human pathology appears clinically quite different from the symptomatology presented by the patient. Visual agnosia, as H. Ey says, is a partial dissolution of an elementary mnesic function, an "instrumental disintegration."* For the same reasons he did not even present verbal deafness. Visual agnosia and verbal deafness in our subject were in ultimate analysis the expression of a total dissolution of his emotional life.

It is through this deep emotional change, quite evident soon after the operation and more clearly definite some 15 days later when the postoperative period was over and it was possible to study the patient's behavior among men and things, that he really appeared demented — a dement who could read, articulate letter by letter, but could not understand the meaning of words; who could write spontaneously only his name; who could speak only in order to satisfy the most urgent needs of his immediate present. He could not remember anything of his past and could make no plan for his future. Hence his serious lack of memory. For MacLean,[27] who proposed the name of "visceral brain" for the limbic lobe, the rhinencephalon (as Herrick suggested) should have the function of activating mnemonic mechanisms.

On the other hand, the importance of recent researches made by Penfield[28,29] about the stimulation of the temporal cortex in man cannot be denied. Through

*For Von Monakow and Mourgue[26] visual agnosia also supposes a basis of emotional indifference and should be the result of disorders in the affective sphere.

these stimulations a series of recollections was produced which permitted Penfield to consider the temporal cortices as "a store house of remembered experience." Penfield maintained that, during the stimulation, the remembered event, the subject's thought bound to that event, and the emotion aroused by that same event are all simultaneously reproduced. He expressed the hypothesis that the temporal registration of memory patterns might occur bilaterally. This derives from the fact that no amnesia appeared, not even limited to a group of memories, after unilateral removal of the temporal cortex and particularly not after the removal of the same cortical areas by the stimulation of which the recollection had been produced. Our case, through the serious lack of memory produced, might therefore be considered as the confirmation of Penfield's theory. If, on the other hand, we take into account that Penfield himself never obtained a recollection through the stimulation either of hippocampus or uncus, considerable importance must be given, according to Penfield's scheme, to the removal of the temporal cortex in determining the serious lack of memory. One might think that an impressive change of the emotional behavior had taken place because of the removal of rhinencephalic structures, according to Papez's scheme, and that lack of memory was due to removal of the temporal convolutions according to Penfield's scheme. Such a division may be arbitrary and artificial, but one should not forget that in Klüver and Bucy's experiments the bilateral ablation of the lateral temporal cortex alone did not determine any considerable change of the animal's behavior. The same is true concerning behavior and memory in human beings after surgical bilateral removal of the temporal cortices.[14,18] On the other hand, one cannot deny the great physiologic importance of the results obtained by Penfield by stimulation of the human temporal cortex.

With regard to the modifications of sexual behavior, hypersexuality was analogous to that observed by Klüver and Bucy in monkeys and by Schreiner and Kling[9] in cats. The latter authors put forth the hypothesis that the amygdaloid complex must regulate in some way certain endocrine mechanisms connected with sexual activity. This hypothesis is based on 1) the late appearance of any change in sexual behavior with regard to emotional behavior; 2) the immediate abolition of hypersexuality after subsequent castration; and 3) the fact that hypersexuality did not follow a preventive castration. In our opinion, without excluding possible endocrine mechanisms, hypersexuality, like bulimia, should be an inevitable consequence of the abolition of interhuman contacts, which reduce the patient to a simple vegetative being preoccupied only to feed himself and to satisfy, in the simplest way, his sexual instinct. The deviation from the norms of sexual behavior is still, however, inexplicable.

Finally we should discuss why, in our case, the very reproduction of Klüver and Bucy's syndrome occurred, while in the cases referred to in our introduction (particularly the cases of Paillas and Bailey and co-workers) this syndrome did not take place. Undoubtedly an exceedingly important factor is the patient's premorbid personality, which determines to a certain extent the psychic component of many neurologic syndromes. Also, these operations cannot be closely compared in their results, even

when they have the same topographic limits surgically. Only an accurate examination at necropsy could thoroughly inform us of the actual extent of these various demolishing operations, particularly with regard to the removal of structures which determine the most important symptoms of the complex syndrome of Klüver and Bucy.

SUMMARY

A case of bilateral removal of the temporal lobes in man (including most of the uncus and hippocampus), exactly reproducing Klüver and Bucy's syndrome, is here described and discussed. The syndrome includes: 1) loss of recognition of people, even close relatives; 2) considerable changes in emotional behavior (loss of fear and rage reactions); 3) increased sexual activity, in the form of self-abuse and homosexual tendencies; 4) remarkable changes in dietary habits (bulimia); 5) "hypermetamorphosis"; and 6) serious deficiency of memory.

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Cephalic Tetanus

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TETANUS is a specific infectious disease known since the time of Hippocrates and Aretaeus, who described its symptoms in graphic language. Through the centuries this condition has brought a great deal of suffering to humanity because of its grave prognosis, even after Kitasato[1] proved experimentally the specificity of the tetanus antitoxin.

Generalized, localized, and cephalic tetanus are the three clinical forms that have been described. The opportunity of diagnosing and treating a case of cephalic tetanus occasioned our interest in this particular problem. Cephalic tetanus is a condition which results when an injury provides a portal of entry in the region of the head, usually the face. The most frequent site of injury is the eye. However, injury to the face, infection of the ear, and the operative procedure of tonsillectomy have been reported as situations providing a portal of entry for the *Clostridium tetani*. Cephalic tetanus is characterized by a syndrome in which trismus, peripheral facial paralysis, and/or ophthalmoplegia are the prominent manifestations. The facial paralysis may be complete or incomplete, but it is peripheral in type. The opththalmoplegias are most commonly due to oculomotor nerve paralysis; however, trochlear or abducens nerve paralyses have been described. The incubation period is variable, but it is usually about a week, and trismus usually precedes the facial paralysis and ophthalmoplegia.

The syndrome of cephalic tetanus may remain limited to the head, or the disease may spread to involve the remainder of the body and result in the development of generalized tetanus. The latter situation is the most frequent fate of cephalic tetanus, and that is the reason why many investigators consider cephalic tetanus as the first phase of generalized tetanus in which the portal of entry is discovered in the head. There are only 13 cases of cephalic tetanus reported in the American literature, and in this small group only one case had tetanus which remained limited to the head. The following report, therefore, presents the second case of tetanus limited to the head to be described in the American literature.

CASE REPORT

History. A five year old white girl was admitted to the neurologic service of the Jefferson Medical College Hospital on April 7, 1953. Her present illness dated back to March 21, 1953, at which time she was playing with other children throwing sticks into a pile of horse

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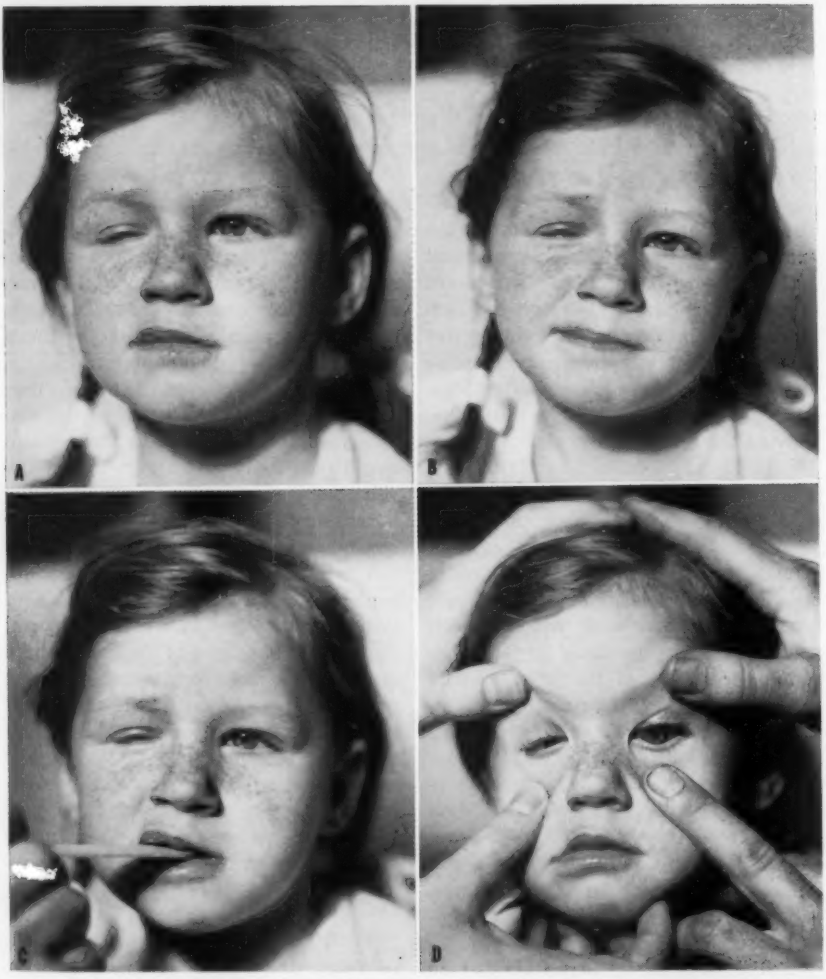

FIG. 1. Significant neurologic findings noted upon hospital admission: *A*, left facial paralysis. *B*, right facial spasm. *C*, trismus. *D*, left abducens paralysis.

manure; she was suddenly struck by one of the sticks near the external canthus of the left eye. There was a small laceration of the eyelid and of the conjunctiva over the sclera, associated with slight bleeding. In about half an hour after the injury there was evidence of swelling around the eye and the patient complained of slight pain. The eye remained swollen for several days but this had almost completely subsided when, on March 27, the child began to bump into objects around the house and complained of double vision. The next day she had difficulty in opening her mouth which persisted and progressed until the date of ad-

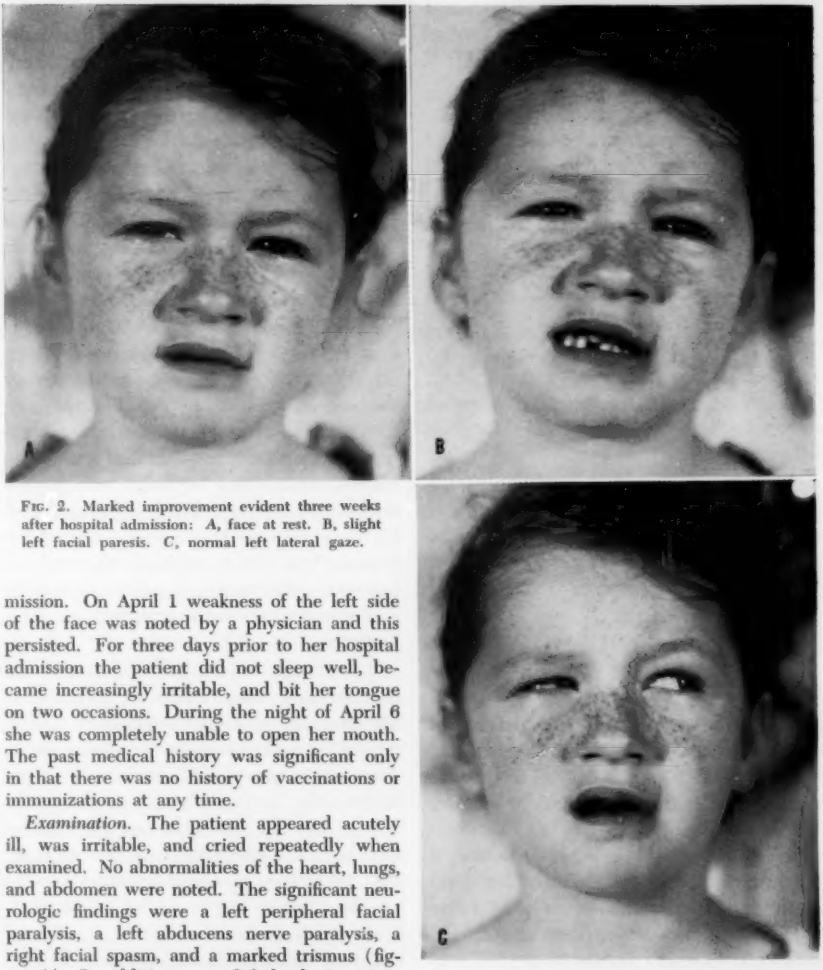

FIG. 2. Marked improvement evident three weeks after hospital admission: *A*, face at rest. *B*, slight left facial paresis. *C*, normal left lateral gaze.

mission. On April 1 weakness of the left side of the face was noted by a physician and this persisted. For three days prior to her hospital admission the patient did not sleep well, became increasingly irritable, and bit her tongue on two occasions. During the night of April 6 she was completely unable to open her mouth. The past medical history was significant only in that there was no history of vaccinations or immunizations at any time.

Examination. The patient appeared acutely ill, was irritable, and cried repeatedly when examined. No abnormalities of the heart, lungs, and abdomen were noted. The significant neurologic findings were a left peripheral facial paralysis, a left abducens nerve paralysis, a right facial spasm, and a marked trismus (figure 1). In addition, an ophthalmologic survey revealed an exposure punctate keratitis of the left eye.

Laboratory studies. Complete blood count, urinalysis, blood urea nitrogen, blood phosphorus, blood culture, serology, cerebrospinal fluid, tuberculin skin test, and heterophile antibody titer were all normal. Roentgenograms of the cervical spine, skull, orbits and optic foramina, temporo-mandibular joint, and mandible were all negative. Cultures made from the eye were negative. However, cultures made from the end of the sticks with which the children were playing, as well as three specimens of horse manure, were all positive for *Clostridium tetani.*

Course in hospital. Upon admission the patient was suspected of having tetanus and was treated accordingly, with the expectancy that

generalized tetanus would ensue. Her course in the hospital was afebrile and on repeated examinations there was no evidence of generalized tetanus. She made a fairly rapid recovery. On the third day the patient was able to open her mouth enough to permit oral feedings. On April 14, 1953 the trismus had completely disappeared; however, the left abducens and facial nerve paralyses persisted. On April 24, 1953 the extraocular movements were normal in all directions but there was still evidence of a slight facial weakness on the left (figure 2). The patient was discharged in good condition on May 5, 1953 and has remained in good health since that time.

Therapy. Tetanus antitoxin in a dose of 50,000 units was administered daily intravenously in a slow drip during the first two days in the hospital. In addition, 15,000 units daily were given intramuscularly. On the third day 40,000 units were given intramuscularly, and thereafter 20,000 units daily for five days. Penicillin was administered in a dose of 300,000 units twice daily for two weeks. Bacitracin ointment was used locally in the left eye. An occasional dose of paraldehyde was given by rectum as a sedative during the early part of the hospital stay. The patient was fed intravenously during the first two days in the hospital.

DISCUSSION

According to Wetzel,[2] the first report of tetanus following eye injury was made in 1847 by Pollock.[3] Edmond Rose[4] was the first one to describe cephalic tetanus. He drew attention to a triad of symptoms: 1) the wound in a region supplied by a cranial nerve; 2) facial palsy, generally on the injured side; and 3) tetanic spasm of the masseter, face, throat, and neck musculature. In the twentieth century several series of cases have been reported. Schneider[5] cited 19 cases while Castelain and Lafergue[6] cited 22 cases.

The problem of tetanus following eye injury and the use of prophylaxis was considered by Cogan,[7] who also cited 29 cases from the literature. The number of such cases of tetanus increased to 31 with the report of Wetzel,[2] who also reviewed the literature on cephalic tetanus. However, the most comprehensive review of the literature and the most complete paper concerning this problem is that of Jayme-Goyaz.[8]

The first case of cephalic tetanus to appear in the American literature was reported by Willard[9] in 1895. This was followed by the report of Eastman,[10] in which three previously unrecorded cases, as well as the case reported by Brown,[11] were described. A case of head tetanus was reported by Butler[12] who attributed the facial paralysis to a neuritis of the seventh nerve. In 1941 Tribby and Long[13] reviewed the American literature on cephalic tetanus and cited the case of otogenous cephalic tetanus described by Bishop, DuBose, and Hamlin,[14] as well as the case described by Hyman[15] in which cephalic tetanus followed tonsillectomy. A case of unilateral cephalic tetanus was reported by Alajouanine.[16]

The cause of cephalic tetanus, like that of any other form of tetanus, is an infection due to *Clostridium tetani.* Cephalic tetanus is a rare condition when it is compared with other forms of tetanus. It was considered rare even before the prophylactic use of tetanus antitoxin for prevention of the disease. The incidence of cephalic tetanus as to age and sex is the same as in generalized tetanus. In the vast majority of cases of tetanus the agents which provide the source for infection have been contaminated by direct contact with horses or with the ground presumably contaminated by their excrement. In the majority of instances, cephalic tetanus follows an injury of the face and in the distribution of the facial nerve—namely, at the rim of the orbit, root of

the nose, superciliary arch, eyelids, or ocular globe; however, in rare instances the throat or even the ears may serve as the portal of entry.

Local conditions in the wound necessary for the proliferation of the organism causing tetanus are such as to produce an oxygen reduction potential far lower than that in normal living tissue. Such a requirement may be satisfied by the presence in the wound of other kinds of bacteria, the common one of necrotic tissue, and/or the presence of foreign particles of various kinds. After a fall in the oxygen reduction potential, tetanus spores may continue in a dormant but viable state for several months. In 1890, Faber[17] showed that *Clostridium tetani* was capable of secreting a soluble toxin which persists after filtration and, when injected into experimental animals, produces the picture of tetanus. This toxin is a protein substance with a strong neurotoxic property acting mainly in the motor nerve cells of the spinal cord, the medulla, and the pons.

In a consideration of the pathogenesis of cephalic tetanus there are several questions to which accurate answers are difficult to find. For example, this condition shows paralytic and contraction phenomena simultaneously. Also the problem of determining whether sensory or motor fibers are responsible for the conduction of the tetanus toxin to the nervous system is not definitely established. In order to explain the paralytic phenomena several theories have been proposed. Rose[4] mentioned two theories, one called the asthenic theory and the other called the mechanical theory. The first one was abandoned very early due to a lack of support from a clinical standpoint. The mechanical theory was an attempt to explain the facial paralysis, and Rose proposed that the toxin irritates the facial nerves causing an agglutination of the nerve and consequently a strangulation at the level of the foramen in the mastoid process. This hypothesis was not confirmed by autopsy findings which showed no evidence of compression of the nerve at the foramen. Sereins[18] in 1880 proposed the reflex theory based on the view that the irritation of a sensory nerve such as the trigeminal stimulates the motor nucleus in the vicinity with resultant paralysis. Zak's[19] case of paralysis of the trochlear nerve following injury to the foot brought serious objections to Sereins' theory. Albert[20] accepted an infectious theory as the explanation for the facial paralysis. However, the work of Roberts,[21] Schnitzler,[22] Caird,[23] and Bernhardt[24] favors the view that the paralysis of the cranial nerves is due to central origin as they were unable to discover any lesion in the peripheral nerves. Nerlich[25] found numerous changes of varying intensity in several bulbar nuclei. Preobarzhenski[26] and Lortat-Jacob[27] also found the above changes on the same side as the paralyzed facial nerve. However, none of these studies explain the occurrence of ophthalmoplegias on the side opposite to the injury.

The best explanation for the problem of contraction and paralysis was given by Brunner.[28] He produced experimentally hemicontraction and paralysis on the side into which he had inoculated tetanus toxin. His conclusion was that the toxin first caused a short contraction of the muscles followed by a paralysis, with the action of the toxin depending upon its virulence and upon the local condition for absorption. The local condition may provide for a slower absorption and hence a longer action upon the

nerve ends with resultant paralysis. He believed that it was a local action upon the facial nerve in contrast to the action upon the trigeminal nerve which the toxin reached by the blood stream. In this way he explained the paradoxical combination of contraction and paralysis, but this is inconsistent with the fact that tetanus follows a nerve-borne spread instead of a hematogenous spread. Worms[29] accepted the view of Brunner that the action of the toxin depended on the virulence of the toxin; however, he admitted that the paralysis is of nuclear origin and inferred that the affinity for the toxin resides in the ganglion cells of the nerve involved. The experiments of Lavergne and associates[30] support the theory of Brunner and the view of Worms; however, the action of the toxin was demonstrated to be dependent upon the dose rather than the virulence. Working with experimental animals, they injected tetanus toxin into the zone innervated by the seventh nerve, producing contraction or paralysis depending upon the dose. The larger doses caused paralysis while the smaller doses caused contraction.

The question whether the motor or sensory fibers absorb and carry the toxin to the central nervous system remains uncertain. Meyer and Ransom[31] believe that the motor nerves are better conductors. Marie and Morax[32] believe that the sensory fibers absorb the toxins in lesser amounts than do the motor. Courmont and Doyon[33] and Autokratow[34] believe that the motor and the sensory nerves absorb and conduct the toxin equally well.

In the majority of cases of cephalic tetanus with ophthalmoplegia, according to Worms,[29] the toxin is conveyed to the brainstem by the oculomotor nerve. His view was based on the observation that in these cases the injury is situated in the region innervated by the oculomotor nerve. In our case it is interesting to note that the ophthalmoplegia consisted of an abducens nerve paralysis, and this may possibly be related to the fact that the injury occurred near the external canthus and external side of the eyeball. It is tempting to speculate with the idea that the toxin was conveyed primarily from this nerve to its nucleus where toxic changes were responsible for the paralysis.

The presence in our case of facial paralysis on the side of the injury and of facial spasm on the side opposite to the injury may be due to the fact that the nucleus on the same side received a larger dose of toxin than the one on the opposite side. The most likely reason for the larger dose is the relative proximity of the toxin to the nucleus of the same side.

The pathology of tetanus has been described by different investigators, with a great deal of variation in the reports as to the site and degree of the lesions. The changes observed have been regarded as reversible by some. One of the best studies on the pathology of tetanus is that of Baker.[35] He states that the reason why tissue changes often are not microscopically discernible is the fact that tetanus is often so fulminating in its course that insufficient time elapses for the changes to become noticeable. His observations indicate that definite changes appear within the central nervous system whenever tetanus has existed for more than three days. Apparently before the fifth day the changes are confined to the nerve cells and consist of mild swelling and chromatolysis. However, if the disease continues beyond the

fifth day more extensive changes may occur, including perivascular demyelinization. According to Baker, in certain cases of tetanus the toxin apparently has a specific affinity for certain cranial nerve nuclei producing definite and irreversible changes. In the case he reported in 1943,[36] the pathologic lesions in the motor nucleus of the trigeminal nerve and in the dorsal nucleus of the vagus nerve correlated well with the patient's clinical picture.

The pathologic studies in cases of cephalic tetanus were reviewed by Jayme-Goyaz.[8] It is noteworthy that several investigators have reported changes in the cranial nerve nuclei, while others considered these changes as inconsistent and without specific significance. Although more investigation is necessary to establish definitely the pathology of cephalic tetanus, it would appear reasonable to assume that the lesions in such cases are confined to the brainstem nuclei and are similar to those described by Baker.[36] Completely satisfactory answers are not yet available to the questions why only some cases of generalized tetanus develop cranial nerve involvement and why some cases of cephalic tetanus remain limited to the head.

The diagnosis of cephalic tetanus should not be difficult if the patient presents himself with a history of injury involving the face, followed by the onset of trismus and with the evidence of facial palsy with or without ophthalmoplegia. However, the diagnosis can be very difficult to establish if the patient comes with the same history of facial injury and the evidence of ophthalmoplegia without trismus. Likewise the diagnosis may be difficult in cases such as ours in which the patient complained of diplopia before the onset of trismus. Although a definite diagnosis cannot be established immediately in such instances, it should be given serious consideration in view of the high mortality rate in tetanus.

As in generalized tetanus the progress of cephalic tetanus may be classified as acute, subacute, or chronic. If the course of illness is acute and fulminating, the prognosis is poor. However, if the evolution is slow the chances of recovery are more favorable. It may also be stated that the shorter the incubation period, the worse the prognosis will be. In cephalic tetanus when the disease spreads and becomes generalized tetanus, the prognosis is worse as compared with the cases in which the tetanus remains limited to the head. The duration of the illness varies from two days to as long as ten days. The facial nerve paralysis and the ophthalmoplegia may disappear at the same time as the trismus subsides or may persist for several days or even weeks as in our case.

The mortality rate of cephalic tetanus is very high. Castelain and Lafergue[6] reported four survivals out of 22 cases. Schneider[5] reported two cases which survived out of a total of 19 cases. Wetzel[2] reported a mortality rate of 80 per cent in cases of tetanus following eye injuries.

The treatment of cephalic tetanus should consist of essentially the same measures as those used in the treatment of generalized tetanus. It is beyond the scope of this paper to review in detail the extensive literature dealing with the treatment of tetanus. The therapy may be considered from a prophylactic and active therapy standpoint. As to prevention of tetanus, our experience would not be opposed to the view of Cogan[7]

who stated that the routine use of prophylaxis against tetanus following eye injuries was not necessary unless the agent was in direct or indirect contact with horses. However, the opinion of Wetzel[2] would seem more appropriate and we are inclined to support his view that tetanus antitoxin should be used routinely in cases of injury to the eye.

Active therapy in cephalic tetanus as in generalized tetanus should be aimed toward: 1) the neutralization of the toxin; 2) the local care of the wound; 3) supportive measures; 4) the prevention and control of convulsions; and 5) prophylaxis against secondary infections. We believe that the combination of intravenous and hypodermic use of antitoxin affords the best chance for recovery in these cases. Our experience would indicate that care of the local wound should include adequate cleansing of the affected eye and the use of antibiotics locally and systemically. However, it has been shown by others that injuries to the eye which result in tetanus are usually associated with panophthalmitis. Wetzel[2] felt that enucleation was indicated because seven of his cases recovered following this procedure, and this form of treatment may be necessary for cases in which a panophthalmitis is present. Our case would seem to provide a basis for opposition to the view of Cogan[7] that the eye should be removed before the development of panophthalmitis. Our patient suffered an eye injury, developed cephalic tetanus without panophthalmitis, and recovered without enucleation of the eye. Therefore, it would seem that, if the local infection is not serious and if antibiotics are used intensively, enucleation may not be necessary in all cases.

The prevention of convulsions and the control of spasms is a difficult problem. In our case, except for the feeding problem during the first two days of hospitalization, there were no serious convulsive manifestations. Enthusiastic reports as to the use of Mephenesin are found in the recent literature. However, most of these reports deal with relatively few cases. On the other hand, investigators have shown that the use of Mephenesin is not sustained and cases are reported in which its use was of no avail. The use of curare is not generally accepted. Taylor[37] favored the use of curare, but Cole[38] reviewed this problem and concluded that the use of curare would only be justified if it could be proved that it was more effective and without more risk than sedatives such as paraldehyde and barbiturates. He stated that it should be used only when the sedatives failed and under carefully controlled conditions. It is our considered opinion that the use of curare would be quite dangerous in cases of cephalic tetanus, because it may result in respiratory embarrassment in situations where the medullary centers are already affected by the tetanus toxin.

The use of antibiotics, particularly penicillin, in the treatment of tetanus has been advised by several previous investigators. It will suffice in this paper to advocate their use at least as a prophylactic against secondary infection, if not as an agent against the *Clostridium tetani*.

SUMMARY AND CONCLUSIONS

A five year old girl with the syndrome of cephalic tetanus is described. The conspicuous neurologic manifestations consisted of trismus, right facial spasm, and paralysis in the distribution of the left abducens and facial nerves. A note-

worthy recovery was obtained in this case and serves as a basis for the consideration of treatment in such instances.

The literature is reviewed with special reference to pathogenesis, and it is concluded that tetanus is conveyed to the nervous system centripetally via nerve trunks and within the neuraxis may spread cephalad and caudad. In the case of cephalic tetanus the toxin would be transmitted to the brainstem by sensory or motor nerve fibers or both. The reason why there are paralytic phenomena in cephalic tetanus and not in other forms of tetanus must be left open to further investigation.

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Examination of the Sensory System in Patients After Hemispherectomy

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THE PURPOSE of this report is to present data obtained from sensory examinations on a series of eight patients who had unilateral cerebral hemispherectomies. The operative procedure was done for the purpose of controlling severe intractable convulsive seizures. Seven of the patients had infantile type hemiplegias, and in the other hemiplegia developed at the age of 28 and was secondary to scarring following removal of a glioma. Seven of the eight patients were institutionalized preoperatively because of their disability and were mentally deficient in varying degrees. Consequently it was not always possible to evaluate accurately loss in the various modalities of sensation. In this report a composite of our interpretation along with two illustrative cases will be presented.

It is appreciated that the term "hemispherectomy" may be inappropriate because one entire half of the cerebrum is not removed. Much of the basal ganglial region is left intact. The term is used only because of apparent common adoption. The operative procedure consisted of removal of all the cerebral cortex, the corona radiata, the basal ganglia lying external to the internal capsule, and, in five of the eight cases, the entire caudate nucleus. In the other three the head of the caudate nucleus was not removed. The incision was carried along the internal capsule, leaving the thalamus intact.[1]

Preoperative examination of this series of patients usually revealed diminished response on the involved side to all modalities of sensory stimulation. It was felt that this diminished response was not a lessened sensitivity to stimuli but rather a slowness in perception or recognition of the stimulus. In none was there any preoperative evidence of complete loss of any of the modalities of sensation. Testing was carried out for light touch, superficial pain, temperature, position sense, vibration, deep (tendon, muscle, periosteal) pain, and stereognosis (two point discrimination, weights and shapes of objects, number writing).

Postoperative sensory examination revealed a relatively minimal change from the preoperative status. Even in the very early postoperative period both superficial and deep pain could be accurately

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perceived and located. Hemispherectomy apparently did not alter this ability. Light touch was also well defined early, although in this type of sensation there was a more definite difference between the two sides. There seemed to be a diminution of the finer discriminative powers of touch perception rather than any actual lack of perception. Even the very lightest touch stimuli with fine hair or cotton could be perceived, but stimuli of this sort could not always be differentiated from more coarse touch. Over a period of several months to a year this ability improved, probably as a result of learning on the patient's part, but it never returned to its preoperative level. During the first three postoperative days the ability to identify the finger which was touched was lost but this ability returned to the preoperative level by the seventh to tenth day. The ability to identify the toe which was touched likewise was lost temporarily but soon returned.

Position sense and perception of vibration did not seem to be altered by hemispherectomy even during the first few days postoperatively. This seems to be contradictory to the observations reported by Fulton and others.[2] The recognition of relative shapes and weights of objects placed in the hand was diminished during the early postoperative period seemingly due to lessened motor function in the hand tested, but as the motor control became more adequate so did the ability to discern accurately the type of article placed in the hand. Two point discrimination was not altered by hemispherectomy except that during the first few postoperative days the patients could not distinguish well numbers written in the palm. This ability returned gradually and was back to normal by the third week.

Testing of the visual fields was extremely difficult. The concept of not moving the point of ocular fixation was not readily understood by the patients so that the visual field examinations may not be accurate. All the patients seemed to have an homonymous hemianopsia and all appeared to have splitting of the macular vision.

CASE REPORTS

Case 1.—This male patient was born April 18, 1923. At the time of birth instruments were used and his delivery was said to have been very difficult. Immediately after birth he had a left hemiplegia, and he began to have grand mal type convulsive seizures during the first week of life. The seizures continued during infancy, then disappeared only to recur at the age of 12 years. Except for the left hemiparesis and the recurring convulsive seizures, he got along reasonably well and was able to graduate from high school. Shortly thereafter the seizures increased in frequency and severity, and because of this plus an increasingly difficult behavior problem it was necessary to commit him to the State School and Hospital at Cambridge, Minnesota. During the following ten years he averaged over 100 grand mal seizures per year. Preoperative neurologic examination in 1953 revealed a well oriented and cooperative 30 year old man with a severe left hemiparesis. The Stanford-Binet intelligence quotient was 86. He had a central type left seventh and a left twelfth nerve involvement. There was a definite left hyperreflexia with bilaterally absent abdominal reflexes and a left Babinski sign. He had a severe left hemiparetic gait, and his left hand was useless although he was very strong at the shoulder and elbow. There was moderate atrophy of the entire left side of his body. Sensory examination revealed no difference between the two sides in any of the modalities tested. A pneumoencephalogram revealed a large subarachnoid cyst in the right frontoparietal area. Carotid angiography revealed no filling of the right middle cerebral artery. On May 4, 1953 the following structures were removed on the right side: the cerebral cortex including the hippocampal gyrus, the corona radiata, the globus pallidus, the

putamen, and the tail of the caudate nucleus. The head and body of the caudate nucleus were left intact. The line of dissection was carried through the middle of the corpus callosum and the internal capsule. His postoperative recovery was slightly delayed because of a vascular lesion in his right arm produced by inserting a polyethylene tube into the brachial artery at the time of operation. By the twelfth postoperative day, however, he was walking and his right arm was greatly improved. Sensory examination during the immediate postoperative period revealed pain perception to be present on both sides, but less well appreciated on the left (hemiparetic) side. He could accurately identify coins placed in his left hand, and position sense was present but somewhat diminished compared to the uninvolved side. Vibration sense appeared to be intact. Examination three months postoperatively revealed no essential change. During the examination one year postoperatively he stated that he could "feel better" with his entire left side but he could "feel faster" on the right side. Testing confirmed this subjective opinion. At this time pain was appreciated about equally on both sides. His proprioceptive sense in a number of tests was accurate and repeatable, but he seemed to work harder to arrive at the correct answer in interpretation of skin writing. The sensation over his face as well as corneal reflexes were entirely normal bilaterally. Visual field examination revealed a right homonymous hemianopsia with apparent macular splitting.

Case 2.—This patient was born on October 6, 1918. Her mother stated that she had a left hemiplegia at the time of birth. At the age of two she began to have grand mal type convulsive seizures. The convulsive seizures continued throughout childhood and at the age of 20 years greatly increased in frequency and severity. Because of these seizures, the hemiplegia, and a marked personality disturbance she was committed to the State School and Hospital at Cambridge, Minnesota in 1947. During the succeeding years she had from five to ten grand mal convulsive seizures per day. Examination in March 1953 revealed a well developed, slightly obese 33 year old female who was alert and cooperative and who had a Wechsler-Bellevue intelligence quotient of 78. There was bilateral optic atrophy with a complete left homonymous hemianopsia. There was a left sixth nerve paralysis and a bilateral horizontal nystagmus. There was a severe left hyperreflexia with a Babinski sign on that side. The abdominal reflexes were present and equal bilaterally. She had a left hemiparesis much more severe in the arm than the leg. Her left hand was useless, although she could move her fingers, and there was a moderate atrophy of the entire left side of her body. Pneumoencephalography revealed a greatly dilated right lateral ventricle with the entire ventricular system displaced to the right. On March 23, 1953 a right cerebral hemispherectomy was performed. The insula, hippocampus, and caudate nucleus were removed. One-half hour following surgery she was alert and rational. She could move both her left arm and leg. She could perceive both pain and light touch on the left although the stimulus necessary to produce a response was greater than on the right side. Examination seven days later revealed perception of pain, temperature, light touch, and position to be equal on both sides. Proprioceptive senses were still diminished on the left as compared to those on the right. She volunteered that she "could feel better with the left side since the operation." Examination one year following hemispherectomy revealed perception of pain and temperature to be equal bilaterally but light touch was not as well identified as on the uninvolved side. Vibration sense was equal on both sides. Perception of position in her arm, hand, and leg was slightly diminished as compared to the uninvolved side. Two point discrimination and number writing on the skin was slightly decreased on the left but, as in case 1, she could accurately identify numbers if given a little time to think.

COMMENTS

Following hemispherectomy these patients seemed to experience only a minimal reduction in their sensory perception. The reason the loss is relatively minimal after excision of cerebral areas generally considered necessary for the recognition and discrimination of stimuli is not entirely established. The thalamus unquestionably acts as the primary, and probably major, receptive center for perception of pain, temperature, and light touch stimuli. These modalities of sen-

sation remained nearly intact after hemispherectomy. Finer discriminative powers are lost to some extent but not entirely. Tests for stereognosis are only minimally less accurately completed on the involved than on the uninvolved side. This is believed due to the assumption by the remaining (and since early childhood the dominant) hemisphere of these functions usually carried out by the contralateral sensory areas. Nielson[4] has alluded to this assumption of function by his statement that aphasia does not develop in infants from a unilateral lesion regardless of laterality. Similarly, patients with destruction of the internal capsule by vascular lesions (producing anatomically a lesion comparable to a hemispherectomy) retain no such sensory perceptive powers as do these patients with hemispherectomies. An alternative possibility is that in the thalamus there is an ability to discriminate stimuli on a spatial basis. Such localization has been demonstrated in macaques.[2,4] However, the cortex undoubtedly functions to delineate better such tactile stimuli. It is emphasized that in the interpretation of these data it must not be forgotten that the patients in this series were handicapped preoperatively and had been so handicapped for many years. It is believed that because of this fact transference of these data to patients without long standing preexisting neurologic functional loss cannot be done.

SUMMARY

Results are given of examination of the sensory system in patients upon whom "hemispherectomies" were performed. Reports of two typical cases are presented.

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■ The channel of the current which gives the pain when an anterior root is irritated is, consequently, at first towards the trunk of the nerve; then in this trunk toward the periphery, where the recurrence seems to take place, and thence the current returns along the sensitive fibres of the nerve toward the ganglion of the posterior roots, and, at last, passes through the ganglion and these roots, and into the spinal cord.

C. E. Brown-Sequard in *Lectures on the Physiology and Pathology of the Central Nervous System*, published in 1860.

S. S. Korsakoff's Psychic Disorder in Conjunction with Peripheral Neuritis

A Translation of Korsakoff's Original Article with Brief Comments on the Author and His Contribution to Clinical Medicine

Maurice Victor, M.D. and Paul I. Yakovlev, M.D.

FOR A PHYSICIAN, the reading of an original description of a disease is a rewarding experience. Often he finds these classic accounts of disease surprisingly modern in concept and penetrating in clinical perceptiveness. Many of these descriptions are literary as well as medical classics. Unfortunately, certain of these original writings are inaccessible because they are written in a foreign language. The student must depend on a translation in which the spontaneity and contextual richness of the original are often lost. This is most apt to occur when certain passages of these writings are translated in fragments out of total context. In such fragmentary translations, usually made in order to satisfy the momentary needs of a quotation or reference, all the subtler traits and colors of the original are distorted or obliterated. Only a reading of the careful translation of the entire original text of the classic description of a disease entity enables one to understand the development, one might say the ontogeny, of our own contemporary ideas of the disease, and, as a corollary, to discern where errors and misconceptions may have arisen.

These general remarks are particularly pertinent to Korsakoff's description of a unique yet relatively common affection which is now known by the name of Korsakoff's psychosis. Korsakoff wrote in Russian, a language which remains relatively unfamiliar to physicians in other parts of the world. In the course of over half a century many of his original observations and ideas have been misquoted, distorted, or even completely lost in the secondhand treatment of the subject by subsequent writers. It occurred to us that it would be useful to students of clinical medicine, especially to those interested in neurology and psychiatry, to have an English translation of Korsakoff's article of 1889, which represents, in a sense, a final statement of his own views on the

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characteristic mental disorder occurring in conjunction with peripheral polyneuritis.

A few words on Korsakoff himself are appropriate as an introduction. A more detailed biographic sketch by Katzenelenbogen may be found in Haymaker's *Founders of Neurology*. Sergei Sergeievich Korsakoff* (1853-1900) was one of the outstanding Russian clinicians of the nineteenth century. Despite the fact that he died at the age of 46, his contributions to clinical psychiatry were numerous and significant. Besides his classic work on polyneuritic psychosis, he wrote on paranoia and his textbook of psychiatry not only remained a standard textbook for Russian medical students for nearly a quarter of a century after his death, but compared favorably with the best contemporary works in other languages. His lasting fame, however, was acquired by his recognition and masterly description of the mental disorder which now bears his name.

In the years 1887 to 1889 Korsakoff wrote three articles in which he developed his theme. The first of these articles was entitled "The disturbance of psychic activity in alcoholic paralysis and its relation to the disturbance of the psychic sphere in multiple neuritides of nonalcoholic origin." Here, on the basis of observations in 20 patients, he first drew attention to the psychic symptoms that so frequently accompany alcoholic neuropathy. He brought out the idea that the psychic disturbance and the neuropathy represent "two facets of the same disease" . . . . "The pathogenic cause provoking multiple neuritis may affect several parts of the nervous system, central as well as peripheral, and according to where this cause is localized there will be symptoms either of neuritis or of the brain." Because of this close associationship he proposed the name "psychosis associated with polyneuritis," or "polyneuritic psychosis."

It is of interest that the term Korsakoff's psychosis is used today in a restricted sense – connoting a characteristic defect in memory with confabulation. It is apparent, however, from Korsakoff's earliest writings that his patients suffered a much wider range of mental symptoms, including those of delirium and what he termed "irritable weakness" (anxiety, fear, and depression). Memory disturbances were indeed characteristic, but not in all patients, and in some instances were present only as a phase in a mental illness that included the other symptoms as well.

A second article (1889), entitled "A few cases of peculiar cerebropathy associated with multiple neuritis," was largely concerned with the reporting of additional cases. It was in this article that Korsakoff brought out the capital fact which is still not fully appreciated today – that neuropathy need not accompany the characteristic mental syndrome. In his own words: "At times . . . the symptoms of multiple neuritis may be so slight that the whole disease manifests itself exclusively by psychic symptoms." In this article he stated his views on the etiology of the mental illness: "I call this form toxemic, because I consider the disturbance of brain in this form closely connected with some form of toxemia. It is connected with the presence in the blood of some

*In his publications in German, Korsakoff spelled his name with a double "f", following the usage prevailing then in spelling Russian names phonetically rather than in transliteration from Russian spelling – Korsakov.

poisonous substances, some toxins." He suggested the name "cerebropathia psychica toxaemica."

The third article in this series was published in 1889 and is the one which has been translated and reproduced in its entirety below. Lucid of argument, simple and direct in style, it represents the consummation of Korsakoff's ripened clinical experience, and sums up his thoughts on various subtler aspects of the subject.

Psychic Disorder in Conjunction with Multiple Neuritis*

(Psychosis Polyneuritica s. Cerebropathia Psychica Toxaemica)

By Dr. S. S. Korsakoff

In two articles, one published in the *Vestnik Psichiatrii*** in 1887, the other in *Yejenedelnaja Klinicheskaja Gazeta*† this year, I have described a special *form of psychic disorder* which occurs *in conjunction with multiple neuritis*. I consider it necessary once more to draw attention to this form of disorder because in my opinion it is insufficiently known to physicians, and yet it is encountered not only by psychiatrists but also by practitioners of other specialties. I would say even more; cases of this form of disorder most frequently come under the observation not of the psychiatrists but of internists and gynecologists, because the form of psychic disturbance under consideration here usually develops in the course of other diseases – post partum, during acute infections and some chronic diseases. In almost all cases which I happened to observe, symptoms of this form of mental disturbance baffled the attending physician and so a specialist in nervous diseases was called in consultation. However, I must say that this form of psychic disturbance is as yet little known even to the specialists. In any case, in the foreign literature there exists no description of this disorder as a separate entity.

Yet the disease is in itself highly characteristic. To begin with, the conjunction of psychic disorder with manifestations of multiple degenerative neuritis is characteristic. In almost all cases of this disease it is possible to note signs of multiple neuritis. It is true that in some cases the signs of multiple neuritis are mild. But in other cases the manifestations of neuritis – paralyses, contractures, muscular atrophies, pains–are so prominent that they even overshadow the psychic disorder. Then, in addition to being associated with manifestation of neuritis, the symptom complex of psychic disorder is in itself characteristic; especially characteristic is a derangement of memory and of the association of ideas. All this makes the disease so peculiar that one may wonder why it had not been hitherto described. I explain this by the fact that, as I have said, this disease usually occurs in the course of other diseases to which all the attention of the physician is directed and thus the complications occurring in the nervous system are not properly appraised.

In fact, it is often difficult to notice the beginning of the disease. Because usually it complicates other grave diseases, such as for example, postpartum affections, typhoid, and the like, the initial symptoms of this disease are easily mistaken for natural weakness, exhaustion of the nervous system, or cerebral anemia. The story usually begins with vomiting which may sometimes be very persistent and then extreme weakness develops. If previously the patient was able to walk, he begins to stagger, the gait becomes insecure, and finally he cannot get up at all and is obliged to remain in bed. Then paralyses of the lower extremities become noticeable, affecting particularly frequently the extensors of the thighs and movements of the toes and ankle. Quite

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**S. S. Korsakoff: Disturbance of psychic function in alcoholic paralysis and its relation to the disturbance of the psychic sphere in multiple neuritis of non-alcoholic origin. Volume IV, fascille 2.

†S. S. Korsakoff: A few cases of peculiar cerebropathy in the course of multiple neuritis. No. 5, 6, 7–1889.

frequently, following paralysis of the legs, the paralysis occurs also in the arms in which movements of wrists and fingers are first affected. Frequently along with these symptoms pains in the legs and arms occur, marked wasting of muscles develops, electric excitability of muscles becomes lost, contractures develop, and sometimes edema occurs. Usually the patellar reflexes disappear early. In severe cases complete paralysis of the extremities and even of the trunk, bladder, and diaphragm may develop and, as a result of disturbance of the activity of the vagus nerve, paralysis of the heart may occur.

Simultaneously with these symptoms representing the manifestations of multiple degenerative neuritis, symptoms of psychic disorder also develop. At first these are not striking and are considered to be signs of simple irritability or depression of the activity of the nervous system in relation to general weakness. In fact, the patients at first appear either extremely capricious and demanding or, on the contrary, very apathetic and listless as is generally true of very tired people. Later, however, some symptoms usually appear which compel one to admit that he is not dealing here with an ordinary form of nervous weakness. These symptoms appear either in the form of an intolerable irritability and an extreme restlessness, or in the form of attacks of violence with confusion, or in the form of an extreme depression of psychic activity with a profound impairment of memory. As one scrutinizes attentively the psychic symptoms one may then note many interesting details which are highly characteristic for the diagnosis of the disease. Properly speaking, the psychic symptoms do not manifest themselves in the same manner in all cases of the disease which I am describing. In some they are more prominent, in others less; in some a certain set of features predominates, in others, another. Summing up the observations of many cases of this disease, one may conclude that in some of them the predominant features are increased irritability and agitation, with relatively good preservation of consciousness; in other cases, on the contrary, confusion predominates, either apathetic or associated with excitement; and finally, in a third group, a characteristic disturbance of memory – a peculiar form of amnesia – stands in the foreground.

When the psychic disorder consists of a heightened impressionability and irritability, then it manifests itself mostly as an extraordinary agitation, anxiety, and indefinable fear. The patient cannot rid himself of obsessive anxious thoughts; he expects something terrible to happen – either death, or some kind of seizure, or he himself does not know what; he is afraid to be alone, constantly calls for people to stand by him, groans, and laments his fate. At times there are wild shouts, hysterical-like episodes during which the patient is capricious, upbraids the people around him, throws things at members of his household, beats his chest, and so on. The agitation is particularly severe at night; patients are usually almost sleepless and disturb the sleep of others; they constantly call for help, demand that someone stay with them, help them to change position, entertain them, and so on.

With all that, consciousness not infrequently remains fairly clear for a long time. However, in many instances, after the first days of agitation a considerable confusion appears: the patient begins to mix words, he cannot speak coherently, and confuses facts. Day after day the confusion increases. The patient begins to tell implausible stories about himself, tells of his unusual voyages, confuses old recollections with recent events, is unaware of where he is and who are the people around him. Sometimes in addition, there occur illusions of sight and hearing which confuse the patient still further. At times in this state of confusion the patient is perfectly calm, while at other times he is restless. The restlessness occurs most commonly toward evening: the patient begins to be agitated, becomes demanding, makes preparations to go away somewhere, and grows angry at not being given the effects which he requests. Sometimes the agitation reaches an extreme degree and may amount to an almost complete loss of consciousness.

Together with the confusion, nearly always a profound disorder of memory is observed, although at times the disorder of memory occurs in pure form. In such instances the disorder of memory manifests

itself in an extraordinarily peculiar amnesia, in which the memory of recent events, those which just happened, is chiefly disturbed, whereas the remote past is remembered fairly well. Mostly the amnesia of this particular type develops after prodromal agitation with confusion. This excitement may last several days and then the patient again becomes calm and his consciousness clears; he appears to be in better possession of his faculties, he receives information correctly, and yet his memory remains deeply affected. This reveals itself primarily in that the patient constantly asks the same questions and repeats the same stories. At first, during conversation with such a patient, it is difficult to note the presence of psychic disorder; the patient gives the impression of a person in complete possession of his faculties; he reasons about everything perfectly well, draws correct deductions from given premises, makes witty remarks, plays chess or a game of cards, in a word, comports himself as a mentally sound person. Only after a long conversation with the patient, one may note that at times he utterly confuses events and that he remembers absolutely nothing of what goes on around him: he does not remember whether he had his dinner, whether he was out of bed. On occasion the patient forgets what happened to him just an instant ago: you came in, conversed with him, and stepped out for one minute; then you come in again and the patient has absolutely no recollection that you had already been with him. Patients of this type may read the same page over and again sometimes for hours, because they are absolutely unable to remember what they have read. In conversation they may repeat the same thing 20 times, remaining wholly unaware that they are repeating the same thing in absolutely stereotyped expressions. It often happens that the patient is unable to remember those persons whom he met only during the illness, for example, his attending physician or nurse, so that each time he sees them, even though seeing them constantly, he swears that he sees them for the first time.

With all this, the remarkable fact is that, forgetting all events which have just occurred, the patients usually remember quite accurately the past events which occurred long before the illness. What is forgotten usually proves to be everything that happened during the illness and a short time before the beginning of the illness. Such is the case in the more typical instances of the disease; in others, even the memory of remote events may also be disturbed.

It must be noted that in general, depending on the degree of the illness, that is, the depth of the affection, the amnestic manifestations vary. In milder degrees for example, there may be no complete abrogation of the memory of recent events, only the facts are remembered vaguely, unclearly. In some cases the facts themselves are remembered, but not the time when they occurred. In other cases the forgetfulness affects chiefly the patients' own thought processes, and as a result they do not remember what they have said, and so they constantly repeat the same question. At times, all facts are remembered, yet to recover traces of these facts in their memory, to recall the forgotten, the patients need specially favorable conditions. Inversely, in very severe cases the amnesia is much more profound; here, not only memory of recent events is lost, but also that of the long past. In such cases it most frequently happens that present events disappear from the patients' memory instantly, and instead, some events of decades ago are recollected – as a result the patients confuse old recollections with the present impressions. Thus, they may believe themselves to be in the setting (or circumstances) in which they were some 30 years ago, and mistake persons who are around them now for people who were around them at that time but who are now perhaps even dead. In still more severe forms of amnesia, the memory of facts is completely lost, even the memory of words; the patient forgets his own name and instead of words utters broken sounds. In severe forms of amnesia the confusion of consciousness is greater, and in the extremely severe cases a state of complete unconsciousness may occur.

In this disease the amnesia is not stationary; it may wax and wane. These fluctuations in its degree depend sometimes on incidental circumstances such as the effort of attention, the degree of distress, and so forth. The memory often improves, yet

with fatigue it again becomes worse. But of course, most frequently the intensity of the amnesia depends on the general course of the disease and on the depth of the affection, so that if the disease progresses toward improvement the amnesia diminishes and may entirely disappear; if the disease grows worse, however, the amnesia becomes deeper and deeper and the signs of profound confusion are added to the symptoms of amnesia.

In regard to the confusion, it must be noted that in this form of amnesia a slight degree of confusion is frequently present. This confusion does not involve that which the patient perceives at the present moment but affects only the recollection of the past events. Thus, when asked to tell how he has been spending his time, the patient would very frequently relate a story altogether different from that which actually occurred, for example, he would tell that yesterday he took a ride in town, whereas in fact he has been in bed for two months, or he would tell of conversations which have never occurred, and so forth. On occasion, such patients invent some fiction and constantly repeat it, so that a peculiar delirium develops, rooted in false recollections (pseudo-reminiscences).

Such are the more characteristic traits of the psychic disorder observed in patients suffering this disease. As I have said, along with psychic symptoms, there exist symptoms of multiple degenerative neuritis in the form of paralyses of the lower and sometimes of the upper extremities. Yet it must be particularly noted that symptoms of multiple neuritis are far from being obvious in all cases. There occur instances in which there exist only a hint of these symptoms in the form of slight pains in the legs and unsteadiness of gait. Even the patellar reflexes do not always disappear; sometimes they may even be increased or remain unchanged. Yet, on careful examination some signs of neuritis will always be found, and this will help to establish the diagnosis of the psychic affection.

In this form of the disease, beside manifestations of neuritis there usually exist signs of a disturbance of the entire organism. Thus, almost always there is severe emaciation, frequently there is persistent vomiting and reduced elimination of urine which is as red as the strongest tea. Not infrequently there are manifestations of myositis, sometimes there is a disturbance of cardiac activity (irregular pulse), sometimes edema develops, in women menstruations cease, sometimes a slight rise of temperature occurs, and not infrequently, there is a tendency to pleuritis, and so on.

Beside neuritis and signs of cerebral disturbances, not infrequently there also occur signs of involvement of the spinal cord and of the medulla oblongata (disturbances of speech, disturbance of swallowing); sometimes there are ophthalmoplegia externa, nystagmus, and like manifestations.

The course of the disease and its outcome depend on the intensity of the disease and on the conditions under which it develops. As I have already said, the disease often develops in the course of other acute and chronic illnesses. Not infrequently it occurs in chronic alcoholism and in various other intoxications in general.

Depending on the conditions under which the disease develops, the onset and the course vary. Thus, in alcoholism, the disease frequently begins with symptoms resembling delirium tremens and then follow paralyses and characteristic disturbances of memory. Not infrequently, an onset similar to this occurs also in the postpartum affections: suddenly there occurs an attack of panphobia and intense excitement followed by confusion with disturbance of memory and other symptoms. In other cases, especially in extremely exhausted patients, the disease steals on unnoticeably. Without a sharply demarcated onset there appears a gradually increasing forgetfulness and then follows confusion, which may reach profound degrees.

The outcome also depends on the intensity of the disease and the conditions under which it develops. If the cause of the disease is removable, then not infrequently the outcome is favorable and recovery occurs, even though, it is true, only after a fairly long period of several months, or, even more frequently, after several years. If, however, the cause of the disease is not removable, as, for example, when the disease has developed on the background of tuberculous or cancerous cachexia, then the out-

come in most instances is lamentable. The outcome may likewise be fatal if the intensity of the disease is great and the resistance of the organism weak.

And so, the course and outcome of the disease depend to a significant degree on its etiology, and the etiology of this form of disease is identical with that of multiple neuritis. Thus, almost anything which can cause multiple neuritis may also cause this form of psychic disorder. Inasmuch as multiple neuritis is particularly frequent in drinkers, this form of disorder occurs very frequently in alcoholic neuritis or in alcohol paralysis. In this disease, the psychic disorder which interests us here had already been noted a long time ago by M. Huss, yet all the authors have seen in the psychic disorder nothing closely connected with the neuritis, but have considered the psychosis as a mere complication of the disease due to alcoholism.* Nevertheless, I have shown in my first article on this subject that the very same psychic disorder also occurs in those forms of multiple neuritis in the etiology of which alcohol plays no role. It is precisely this fact which compelled me to connect this form of psychic disorder with multiple neuritis in general, and to look for conditions which provoke it under the same circumstances which also provoke multiple neuritis. Up to the present, however, if one discounts those eight or nine cases of multiple neuritis in which a disturbance of intellect has only briefly been mentioned, there appears in the literature no description of mental disturbances associated with neuritis. I confess it surprises me that to this time there exist no descriptions of cases of nonalcoholic multiple neuritis with sharply manifested psychic disturbances, because I see such cases not infrequently, and now can add several other observations to those which have already been published.

In my articles quoted above, the following cases of multiple neuritis of nonalcoholic origin have been described:

1. A 28 year old woman. *After the birth of a macerated fetus*, there developed a picture of multiple neuritis (paralysis of lower and upper extremities, extremely severe pains, atrophy of muscles, contractures, and so on) and along with this a psychic disturbance set in, beginning with panphobia, extreme anxiety, irritability, attacks of violent delirium, and disturbance of memory. The anxiety subsided after some nine months, while disturbance of memory, gradually diminishing, remained for several years. The paralyses also diminished, but a complete recovery never occurred. The patient died suddenly eight years after the beginning of the illness.

2. A 22 year old woman. Post partum there developed *a parametritis with high fever*. Later there appeared symptoms of severe multiple neuritis (paralyses of upper and lower extremities, pain, atrophy of muscles, contracture) and along with this psychic disturbance set in with confusion and a characteristic disorder of memory. The psychic disturbance subsided in the course of a few months while paralyses diminished very slowly in the course of several years. A complete recovery has not yet taken place.

3. A 28 year old married woman. In October 1884 she became ill with an infection of the pelvic organs which remained without an exact diagnosis and which provoked a high fever (*purulent parametritis was presumed*). In December symptoms of multiple neuritis appeared (paralysis of legs, paresis of arms, atrophy of muscles, contractures, pains). Along with this the psychic disturbance developed: capriciousness, obstinacy, later profound disturbance of memory, and at times attacks of violence with hallucinations and delirious ideas. The psychic disturbance subsided in five months, while paralyses disappeared only in the second year after the beginning of the illness.

4. A 19 year old girl. In August 1885, after a cold, there developed pain in the abdomen, fever, and persistent vomiting and then followed manifestations of multiple neuritis with *multiple myositis* (extreme emaciation, contractures, paralyses). Together with this there was a severe psychic disturbance manifested by profound confusion, incoherence of ideas, excitement, and profound loss of memory. The psychic disorder subsided a year later, whereas movements were completely recovered within three years.

5. A 40 year old man. Following typhus there developed neuritis (pains in various nerve trunks) and profound disturbance of memory of recent past with preservation of lucid consciousness. The multiple neuritis soon disappeared. The disturbance of memory persisted for a long time, although it gradually diminished.

6. A 65 year old man. In July 1886 there

*As a mere manifestation of a chronic alcoholic intoxication (Transl.).

developed symptoms of *intestinal obstruction* (fecal vomiting, persistent constipation, abdominal distention). Within a week after the onset of the illness there developed a gradually increasing impairment of memory followed by profound confusion. There was weakness of the legs, pain on pressure of the nerves, and loss of tendon reflexes. Death occurred one and one-half months after the onset of the illness.

7. A woman, about 30 years old. For a long time she suffered of Basedow's disease and lately of *pulmonary tuberculosis;* furthermore, she had tapeworm. After taking extr. filic. maris there developed persistent vomiting followed by psychic disturbance with intense agitation, acute impairment of memory, and confusion. Along with this there was unsteadiness of gait and depression of patellar reflexes. The patient died about one and a half months after the onset of the illness.

8. A 60 year old man. *Diabetes mellitus.* Since July 1880 there was vomiting, unsteadiness of gait, and gradually increasing weakness of legs with loss of tendon reflexes. Together with this there developed a profound disturbance of memory and reasoning. Improvement began six months after the onset of the illness, and after a year a complete recovery from nervous disorder occurred.

9. A 46 year old maiden. Following an attack of jaundice vomiting developed and two months later a comatose state following which there appeared a profound memory disturbance and confusion. Along with this there were symptoms of multiple neuritis (contractures in toes, pain in nerves and muscles, and other manifestations). The illness almost subsided within two years.

10. A 37 year old married woman. After typhus(?) tuberculous pneumonia developed. In the course of this illness a picture of multiple neuritis appeared (paralysis of upper and lower extremities with atrophy and contracture). Together with this there was a profound confusion and a severe impairment of memory. The patient died a year after the onset of paralyses.

11. A 45 year old woman. She was ill for four weeks with *typhoid fever.* After its termination there developed a profound loss of strength and vomiting followed by an acute disturbance of memory, confusion, and nocturnal agitation. The symptoms of neuritis were slight: unsteadiness of gait and tenderness of nerve trunks on pressure. Symptoms of neuritis disappeared rapidly whereas weakness of memory, while gradually diminishing, persists for the second year.

12. A 40 year old man who had lues. At present there is lymphadenoma with elevation of temperature at times (possibly malaria). At the end of August 1888 there developed a disturbance of memory. Later attacks of violence occurred and these were followed by severe disturbance of association of ideas with a profound impairment of memory. Together with this there was a gradually increasing weakness of the lower and upper extremities and a loss of the patellar reflexes. The patient died one and a half months after the beginning of nervous symptoms.

13. A 46 year old woman. *Fibroma uteri.* Signs of disintegration of the neoplasm had been noted. Together with this there appeared vomiting, profound disturbance of memory, and confusion. Simultaneously there was a gradually increasing weakness, an absence of patellar reflexes, and persistent vomiting. The patient died two weeks after the onset of nervous symptoms.

14. A 62 year old woman with some type of abdominal tumor developed, without evident cause, a persistent vomiting which was followed by apathy, confusion, and a profound disturbance of memory. Together with this there was weakness of the legs, wasting of muscles, tenderness on pressure of the muscles and nerves, and a profound depression of cardiac activity. Two weeks after the onset of this illness there was improvement and eventually a complete recovery.

Such are 14 cases in which I observed this particular psychic disorder combined with multiple neuritis of nonalcoholic origin. (I do not speak of cases of this psychic disturbance associated with alcoholic neuritis – of such I have not less than 30). In all these cases the psychic disorder was sharply in evidence. As to the symptoms of multiple neuritis, these were variable. Thus in some, the picture of multiple neuritis was complete; in others, on the contrary, the manifestations of neuritis were insignificant in comparison to the psychic symptoms. Apparently there also occur such cases in which in the presence of the sharply manifested psychic disorder of the type described above the symptoms of neuritis are almost unnoticeable and consist only of slight pains in the extremities. In my opinion this depends on the circumstance that in some cases the pathogenic agents provoking the psychic disorder and the multiple neuritis cause both, acting equally upon the brain and peripheral nerves; in others these agents act more on the brain,

and in others again almost exclusively on peripheral nerves. Along with this, in all probability, involvement of various parts of the spinal cord and of the medulla oblongata occurs not infrequently.

What may be the pathogenic agents provoking the disease which I am describing? If one examines closely the etiology of the cases described above, then one may note that the causes of the disease are many: here we find the delivery of a macerated fetus, a postpartum septic process, a fecal impaction, typhus, tuberculosis, diabetes, jaundice, lymphadenoma, necrosis of a neoplasm, and finally, altogether unknown causes. If one adds to all the above the fact that the same form of the disease is observed in alcoholism, and also apparently after poisoning with arsenic, lead, hydrogen disulphide, carbon monoxide, ergot, spoiled corn, and so on, then one sees that the causes which can evoke this disease are very diverse. However, if one weighs carefully the significance of these causes, then their action may be reduced to an incorrect constitution of the blood, developing under their influence and leading to an accumulation in the blood of toxic substances which poison the central nervous system — in some cases peripheral, in others central, and most frequently both.

What these toxic substances may be is difficult to say, yet in all probability they are some ptomaines or leukomaines either entering from without or developing under appropriate conditions within the organism itself (typhoid, tuberculosis, fecal impaction, macerated fetus, and so on). And this is why I call this disease *toxemic cerebropathy* (cerebropathia psychica toxemica). One might also call it *psychosis polyneuritica*, but using this designation one must remember that an identical psychic disturbance may occur also in cases in which the symptoms of multiple degenerative neuritis may be very slight or even entirely wanting.

Insofar as the pathologic anatomy of this disease is concerned, this is not yet sufficiently clarified. However, the presence of the multiple neuritis in this form of the disease can be considered as proved beyond doubt. This year, a female patient in whom the described disorder was very sharply expressed died in the Moscow Psychiatric Clinic. She was found to have had a very severe form of multiple degenerative neuritis. The study of the brain and spinal cord is not yet completed, and therefore I am postponing the description of this case for another occasion. At present I will cite two more cases of this affection which I had occasion to observe lately.

The patient, a 24 year old married woman, had several children; the deliveries did not always go well: once there was postpartum fever although without particular disturbance of the nervous system. The patient was always an impressionable, anemic, nervous woman. She hardly ever drank. The present illness began about mid-October of 1888. On October 11 she gave birth to a full term baby, but the next day an elevation of temperature appeared and a postpartum suppurative parametritis set in. The illness has continued to the present. In the genital sphere there were at first only the manifestations of parametritis, but later abscesses appeared in various parts of the body (in the breasts and legs). In November she had penumonia. All this reduced the patient to a state of profound exhaustion and maintained the temperature at a level of about 39° C. until very recently. Only at the end of December the temperature became nearly normal and with this most of the manifestations of parametritis and pneumonia disappeared. There remains only the abscess of the hip which is being constantly treated with an antiseptic dressing.

By the end of October, in addition to the signs of parametritis and pyemia, symptoms of involvement of the nervous system appeared. The patient began to have delirium, she spoke incoherently, and at times was agitated. The character of her psychosis was peculiar. According to the statement of the attending physician, at times she spoke entirely rationally, gave a correct account of everything, and did not confuse anything, so that it was difficult to notice any psychic abnormality; but then, suddenly confusion would begin, delirium would develop, the patient would become restless and beset with fear, she would hallucinate, see dogs and monsters, and attempt to jump out of bed and to tear off her dressings. These attacks usually occurred toward evening when the patient generally became more agitated and alarmed; she constantly summoned people, became tormented by fear, and then an attack of intense anxiety with illusions and hallucinations developed. At first the patient had difficulty in falling asleep and frequently awoke. Awakening, she became restless, again summoned people, shouted, and then again fell asleep for

a short while only to wake up in the same state of anguish. So it continued throughout the whole of November. In December some improvement began: the attacks of violence diminished, she became quieter and much more rational. But, with this improvement the enfeeblement of memory became all the more noticeable. The patient would forget who had visited her; she would forget what she herself had said and so she would constantly repeat one and the same thing, tell the same stories time and again, and ask the same questions. Her sleep continued to be irregular. At times there was vomiting; at times the patient complained of pain in the sacral region; for a time she could hear almost nothing and lost her sense of smell. I saw the patient on December 30, 1888 in consultation with her attending physician, Dr. M. D. Lebedev, and found her in the following state:

Status praesens, December 30: At present there is no great physical weakness which was present formerly. During my visit the patient is able to sit in an arm chair and to hold herself in the sitting position; she converses willingly and speaks fairly loudly. According to Dr. Lebedev, the pelvic process has already terminated. There remains an abscess of the hip which discharges freely. The temperature has been normal for several days. Lately there was no vomiting; appetite is satisfactory, stomach likewise. On examination of the nervous system it is found that although the legs are somewhat weak, there is, however, no paralysis either of the arms or of the legs; the mechanical contractility of muscles is preserved; the muscles are quite wasted. At present the patient hears everything well, recognizes taste and odor, and also sees well; sensations are preserved everywhere. Pressure on nerves (cruralis, ischiaticus, radialis) is associated with considerable tenderness. At times there are spontaneous pains in the legs. However, pains do not disturb the patient as much as the intense pruritus over the lower legs. Patellar reflexes are present but very weak. There is a barely noticeable edema of the ankles. During my visit, at first no clear-cut psychic abnormalities could be noticed. The fact of the matter is, however, that in the presence of a new person the patient generally performs better than she does with familiar people. Because of this her answers to my questions were for the most part fairly correct. However, on continuing the conversation with the patient for a longer time, it becomes evident that her memory is severely affected: she is completely unable to remember what she had been doing today, for example, whether or not she ate anything; she is unable to recollect whether anyone visited her or not. Nevertheless one cannot say that the loss of memory is complete; thus, at times the patient remembers events that occurred today and yesterday, but is unable to specify the time of these events. The patient forgets particularly easily that which she herself had said, and as a result of this she frequently repeats the same thing time and again and asks the same questions.

That which happened before her illness the patient remembers well. She remembers her illness vaguely, although she does remember that she was as though she were out of her mind. She remembers the most recent events most poorly. Nevertheless the loss of memory does not go so far as to cause her to attribute to herself what has never happened. For example, she does not say, as other patients of this type do, that she went out yesterday or today; on the contrary, she realizes that she has been sick for a long time, even though she has forgotten whether she had a baby in October or in November.

From the accounts of those around her, one may judge that toward evening the patient even at present becomes more agitated, more restless, more anguished; she sleeps fretfully, frequently awakens, and summons people. However, lately she has had no hallucinations.

I have not seen the patient since then, but I have heard from Dr. Lebedev that she gradually improved, and toward the spring of 1889 she was completely well: she was able to walk, gained weight, and her memory was restored.

In this case the manifestations of neuritis were comparatively mild. They consisted of pains in the extremities, pruritus, and slight weakness in the legs. The psychic disorder however was very characteristic. This case proves among other things that in many cases the psychic disturbance is incomparably more pronounced than the manifestations of neuritis, which, considered by themselves, can be easily overlooked. It seems to me that such cases fully justify the isolation of this form of psychosis into a separate entity.

In the following case, which I had occasion to see through the kindness of my esteemed colleague, S. N. Zarembo, the neuritis was extraordinarily severe.

The patient was a married woman about 40 years old. She hardly ever drank. She was a lively, active woman who for a fairly long time suffered of rheumatoid arthritis. In 1887 she went to Saki,* later took sea baths, and had a good winter 1887-88.

*A watering resort in the Caucasus (Transl.).

Early in August 1888 she was entirely well. About mid-August, following a cold, she was taken ill with parametritis (pains in the lower abdomen, fever, and other objective symptoms of parametritis). In mid-September, in addition to these manifestations, there appeared symptoms of peritonitis. There were extremely severe pains in the abdomen, vomiting, the temperature rose to 40° C. and remained so for a fairly long time. Dr. S. N. Zarembo was not in Moscow at the time, and for this reason he was unable to tell me what precisely was the matter with this patient. In addition to peritonitis there were manifestations of left-sided pleuritis, and finally there was a left-sided suppurative parotitis which had to be opened. Dr. S. N. Zarembo saw the patient about October 22, 1888, soon after the opening of the parotitis. At that time there was parametrial exudate, a high fever of about 39° C. and very pronounced weakness; at times there was vomiting. On the psychic side he was surprised by the listlessness and apathy of the patient, entirely out of keeping with her usual self. In November the paralytic manifestations began to develop; at first the ankles became weak, the patellar reflexes disappeared, and then the paralysis of the lower extremities became complete. The arm and trunk muscles also became paralyzed. The muscles became extremely wasted and contractures of the flexors developed. At times the patient had attacks of suffocation. At times the heart action became so feeble, that in December, January, and February there was a daily apprehension that the patient might die. In November red spots began to appear on the buttocks and sacrum, which in such cases not infrequently precede the appearance of paralyses. However, bed sores did not develop, possibly because the patient was placed on a rubber mattress filled with cold water.

Simultaneously with the physical symptoms the psychic symptoms also developed. Since the end of October the patient showed noticeable listlessness, apathy, and indifference and in the middle of November there suddenly appeared violent delirium and confusion. The patient shouted, swore, and demanded that she be permitted to dress so she could go to Strelna.* She did not recognize her surroundings and thought that those about her were poisoners. At times she sang and had bouts of laughter. Early in December the incoherent and extremely agitated delirium began to subside, but the confusion and the disturbance of memory persisted for a long time. She did not remember where she was to almost the end of April, she did not remember the names of her nurses, and rapidly forgot everything that happened to her. At night she was extremely agitated, almost sleepless, constantly groaned, called for people, and so forth. However, her memory gradually improved and in May 1889 the patient began to remember her surroundings fairly well.

The manifestations of parametritis also gradually improved and toward May 1889 had almost disappeared. The temperature, which for a long time had remained around 39° C., began to decline in the spring of 1889 and finally became normal, although from time to time, every week or two, there were elevations to 38° C. In May the temperature did not rise above 37.7° C.

I saw the patient June 1, 1889. At that time the psychic symptoms were already slight; the patient knew clearly where she was, who were about her, remembered fairly well what was going on, and related correctly details of her illness. However, in a long conversation one could note anomalies in the psychic sphere. These anomalies chiefly concerned the memory. Thus, in telling of something about the past, the patient would suddenly confuse events and would introduce the events related to one period into the story about another period. For example, telling of a trip she had made to Finland before her illness and describing her voyage in fair detail, the patient mixed into the story her recollections of Crimea, and so it turned out that in Finland people always eat lamb and the inhabitants are Tatars. When I objected, however, she promptly agreed that she had confused the facts. Such muddling of facts not infrequently occurs in this patient, but in most instances she herself notices them. Furthermore, she frequently gives false information in regard to her past illness. Thus, she assures me that she well remembers a physician who came to see her in consultation and describes him as having black hair, whereas he is completely gray. In general the patient does not remember clearly that which occurred during the time of the illness, although gradually the events of her illness become restored in her memory. After a conversation lasting an hour, the patient becomes very listless; one can see that she becomes extremely fatigued mentally. Fatigue in general has a marked effect on the patient, increasing the disorder of memory. At present the patient sleeps satisfactorily, whereas a few weeks ago she slept fitfully and constantly summoned people.

In regard to the peripheral nervous system, the disease is still sharply manifest. In the legs there is paralysis and contracture in flexion at the hip and knee joints. Extension of the knees

*A popular amusement park in the Moscow suburb of that name (Transl.).

to more than 90° is impossible. There are barely noticeable movements in the ankles and toes and barely noticeable extension of the knees. Flexion of the knees is somewhat stronger. Flexion, extension, adduction, and abduction at the hip are possible but extremely limited. The muscles are extremely wasted; generally the legs appear almost deprived of their soft parts, as if only skin and bone and a small amount of flabby flesh in the calves and posterior aspect of the thighs remained.

There is no anesthesia. Pressure on the calves and anterior and posterior aspects of the thighs is extremely painful. Pressure on the nn. cruralis, ischiadicus, and peroneus are also extremely painful. The patellar reflexes are absent. The movements in the arms are grossly disturbed. Contracture is also noticeable in the joints of the shoulder, elbow, wrist, and fingers. The fingers in the left hand had been flexed so that extension was impossible; now however it is possible to extend them. Active movements are very weak and limited. Movements of the right hand are somewhat better. Muscles are extremely thin. Mechanical contractility is noticeable in the right hand.

Trunk muscles are also weak; the patient is unable to turn over, but lately she began to sit. Pressure on the muscles and nerves throughout the body is painful. In the face there is nothing particular. Vision is fair, although the patient complains that at times there is clouding and blurring of her eyes. The pulse is regular but weak. Vomiting has been absent for a long time. Respiration is now free; there is no paralysis of the diaphragm. Urine is voided freely; now it is clear, whereas formerly it was as dark as strong tea; it never contained albumin or sugar. At times the patient has pains in the legs — crushing and aching. At these times she feels worse; she sleeps more poorly and is more agitated. Appetite is generally good, at times even excessive. Generally, the patient is apparently improving.

In this case there were characteristic psychic manifestations as well as characteristic signs of multiple neuritis. It is possible that simultaneously there were present also manifestations of multiple myositis. Generally, this form of the disease can be associated not only with multiple neuritis but also with multiple myositis. This is entirely understandable; lately more and more cases are being described in which together with primary multiple neuritis, there also exists primary multiple myositis. This depends, of course, on the fact that both affections are due to the influence on the tissues of the same pathogenic agents, that is, toxic substances. In one group of cases these toxic substances will affect with predilection the peripheral nervous system and then a picture of multiple neuritis will develop; in other cases the muscular system will be affected and then multiple myositis will appear; if, however, the same toxic substances will act on the cerebrum, then the cerebropathy which I am describing will obtain.

I shall end the description of these two cases with a remark that in both the disease developed in women in the course of affections of the pelvic organs which had apparently provoked a general purulent infection. Among my observations there are not a few such cases with an analogous etiology. This compels me to assume that the gynecologists probably must have many occasions to observe such cases and that the cerebropathy described by me is particularly frequently associated with the neuritides which develop following affections of the pelvic organs. Apparently not all the pathogenic causes which provoke the neuritides have the tendency to provoke also the psychic disorder described here. Thus, I have never seen it in neuritides following diphtheria. Contrariwise, in neuritides of alcoholic origin this disorder is nearly always present. Similarly, it occurs not infrequently in the neuritides following pelvic affections and especially such as are accompanied by symptoms of putrid or purulent infection.

CONCLUDING REMARKS

Sixty-five years have elapsed since this article was written. Over these years many of the fine clinical points made by Korsakoff have been forgotten. Despite this passage of time, only a few points of significance concerning the pathology and etiology of the disease are lacking in the original description. Korsakoff's writings do not include a description of the pathologic changes in the brain.

Actually, however, the neuropathologic substratum of Korsakoff's psychosis still awaits comprehensive study. The few available pathologic studies indicate that the most consistent changes are found in the walls and floor of the third ventricle. Although Korsakoff casually mentioned that brainstem signs occurred in some of his patients, he was unaware of the important association of the mental and the neuritic symptoms which he so clearly described, with the ophthalmoplegia and ataxia described by Wernicke in 1881. Even had he been aware of the close relationship of his syndrome to that of Wernicke's encephalopathy, the possible nutritional etiology of the mental and neuritic symptoms would not have suggested itself therefrom, since Wernicke's syndrome was then regarded as inflammatory in origin. In fact, the entire concept of deprivation in the etiology of disease – the notion that a disease may arise from a lack of a specific nutritional substance rather than from an excess of some deleterious substance (toxin) – had not yet gained credence in the medical thought of Korsakoff's time. Nevertheless, in speculating on the etiology of the clinical syndrome he described, Korsakoff formulated a remarkably modern concept of this disorder. He recognized that the psychiatric and somatic symptoms and the central and peripheral neurologic signs of the disorder were merely different manifestations of a common pathogenic mechanism, and, therefore, probably of the same etiologic origin. In this perceptive generalization, he presaged the concept of the nutritional etiology of disease of the nervous system of which his syndrome is a major manifestation. "In this disease, one and the same pathogenic cause affects not only the peripheral nerves, but also the spinal cord and the brain, and, therefore, to call it exclusively by the name of that system which is affected most frequently is, though practically convenient, nevertheless incorrect. Of course, until we know the nature of the disease, we must of necessity maintain its name, which is, even though incorrect, yet fairly characteristic. Perhaps further researches will show that this disease is not only a disease of the nervous system but also a general disease, and one most probably depending on the development in the organism of some noxious substance disturbing the nutrition of all tissues, but chiefly the nervous system. If we will learn that and if we will learn the nature of this disease, we will be compelled to change the name of multiple neuritis for a more accurate one, and then of course an appropriate name will also be found for this form of psychosis."

Prognostic Value of Sensory Defect in Rehabilitation of Hemiplegics

Charles Van Buskirk, M.D. and David Webster, M.D.

THE PRESENCE of sensory defects in hemiplegia is well known, but the attention it has received has largely been directed toward consideration of the sensory deficit itself, especially as related to localization of the various modalities. The sensory functions of the cerebral cortex and of the deeper centers have been well outlined although not completely defined to the satisfaction of all.[3,4,6,8,13–15] It has been recognized that the motor functions of the brain are dependent upon the sensory functions of this organ to a great extent. This relationship has been considered intimate and close enough to warrant the term sensorimotor cortex.[7,10,11,18] The relationship of sensory deficit to recovery of function and the rehabilitation process has not been considered. Bell and Karnosh[2] studied 80 hemiplegic patients and found disturbed skin sensation in 76 per cent; they also noted that sensory disturbance was twice as frequent in patients with flaccid hemiplegia as in those of the spastic type. Aring,[1] in a consideration of flaccid hemiplegia in man, found sensory defects in all of ten such patients. He mentioned briefly the difficulty of ambulation. Only two of the ten regained the ability to walk. Critchley[6] mentioned in passing the increase in hemiplegic disability which may result where there are concomitant parietal lobe symptoms. Recently Tizard and associates[20] examined 106 children with hemiplegia and found impaired sensation in 50 per cent. They were unable to correlate the severity of the sensory deficit with the degree of motor deficit of the patients in their series.

Because of the reported close relationship of sensory and motor cortex, it seemed worthwhile to study sensation in hemiplegia and to attempt to determine if sensation in these patients had any relation to the rehabilitation process. Such a study was accomplished through serial observations of a few of the more commonly tested sensory modalities.

Thirty-five male patients from the acute neurology and rehabilitation wards of the Minneapolis Veterans Administration Hospital were studied. These patients ranged in age from 31 to 76 and all suffered from hemiplegia. This hemiplegia was the result of a vascular accident in all but two. The etiologies are as follows: thrombosis 28, hemorrhage two, embolus two, arteriovenous malformation one, and trauma two. Serial examinations of pain, two-point discrimination, and vibratory sense were made weekly for periods varying from two to 17 weeks. The disability had been present for from nine days to seven years

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at the onset of the testing period. All of the patients participated or had a trial of participation in the rehabilitation program. As soon as they had reached what was considered maximum hospital benefit, they were discharged from the hospital. A few of the more severely disabled patients were not considered eligible for discharge and remained in the hospital. Length of hospitalization could then be considered as a measure of overall disability, and in this series the length of hospitalization ranged from 17 days to 1,804 days. This method of measuring disability will include such factors as the mental state and general physical condition as well as the neurologic disability, all of which are important in the rehabilitation process.

The sensory determinations were made weekly from homologous areas of the upper extremities. Pain threshold determinations were made from the midpalm of the hands, blackened with india ink, utilizing radiant heat applied over a circular area of 1 square centimeter. The radiant heat was derived from apparatus somewhat similar to that of Hardy and co-workers[12] except that the heat arose from a constant temperature source. The amount of heat was controlled by a revolving shutter, the apertures of which could be varied while the shutter was revolving at a constant speed. This method of varying the intensity of the radiant beam without changing its frequency distribution was considered technically superior to the usual method of varying the temperature of the projection bulb filament, since it permitted accurate and direct measurement of relative intensities with a simple photocell apparatus. Vibratory sense was measured by the use of a standard tuning fork of 128 vibrations per second. This fork was activated maximally using a standardized method. At the same time a switch was thrown automatically which simultaneously activated an electric timer. This timer continued in operation until the patient indicated that he no longer perceived the stimulus. The vibratory stimulus was applied to homologous areas of the wrists. Two-point discrimination was determined by a dull pointed compass from homologous areas over the dorsum of the hands. The determinations were made after practice sessions to be certain that the patient understood what was expected. The final determination was taken to be the average of three consecutive trials. The weekly determinations were then charted and the results for the two sides could then be compared. When the determinations for both sides were identical or very close, sensation was considered to be relatively unimpaired or to have returned to normal as far as the sensory deficit resulting from the cerebral accident was concerned.

On routine neurologic examination, 26 of the 35 patients or 71 per cent were reported to have impaired sensation. On testing, using the methods outlined above, 29 or 80 per cent had impaired sensation. One of the group on routine neurologic examination was found to have impaired pain sensation, but when entering the testing situation two weeks later was found to have intact sensation. On consideration of the individual modalities, 63 per cent had impaired pain sensation, 65 per cent had impaired two-point discrimination, and 62 per cent had decreased vibratory sense. Of those with impaired pain sensation, 23 per cent exhibited recovery of this modality; in 46 per cent, two-point discrim-

ination returned to normal; and in 20 per cent, vibratory sense returned to normal. The times at which these modalities returned to normal following the cerebral accident were two months for pain, with a range of from one and one-fourth months to two and three-fourths months; one and one-half months for two-point discrimination, with a range of from one month to two months; and four and three-eighths months for vibratory sensation, with a range of from three months to five and three-fourths months.

It was found that patients with intact sensation had an average hospital stay of 68 days. On the rehabilitation service, half of these obtained a satisfactory result and half achieved a fair result. Those who exhibited recovery of sensation had an average hospital stay of 76 days and achieved a satisfactory result in rehabilitation. Patients who failed to recover one or more of the modalities had an average hospital stay of 236 days. The majority of these patients achieved a poor result on rehabilitation. The average hospital stay for patients who failed to have return of pain sensation alone was 139 days, for vibration alone 59 days, for vibration and two-point discrimination only 160 days, for pain and two-point discrimination only 140 days, for pain and vibratory sense only 120 days, and for all modalities 395 days.

None of the patients in this series had complete loss of any of the modalities tested.

DISCUSSION

The rehabilitation process is concerned primarily with producing an ambulatory individual who is capable of caring for himself and becoming self-supporting. This result can be achieved in the presence of an almost useless upper extremity. Thus rehabilitation depends little on the degree of motor activity on the hemiplegic side. Tizard and associates[20] were unable to correlate the severity of sensory deficit with the degree of motor deficit in children. No attempt was made in this series to find such a correlation. It is apparent, however, that achievement in rehabilitation and length of hospitalization can be correlated with the degree of sensory impairment present. Furthermore, our series suggests that the prognosis is worse if a disturbance of two-point discrimination persists. This modality was not found to be disturbed alone but always in combination with one or both of the other modalities tested. Since two-point discrimination is mediated by the cortex and pain and vibration sense by subcortical areas,[12,13] this observation suggests that disturbed parietal lobe function may be a significant factor in prognosis for rehabilitation. It also suggests that there were no pure cortical lesions in this group but all involved subcortical areas. The latter supposition is further supported by the observation that when two-point discrimination recovered it did so more frequently and more quickly than did the other modalities.

Parietal lobe functions which undoubtedly play a role in rehabilitation of the hemiplegic patient are those which influence motor function of the extremities bilaterally. The symptoms which may result from a disturbance of these functions have been discussed fully by Critchley and consist of constructional apraxia, tactile agnosia, somatagnosia, and visual agnosia. Any of these could seriously disturb the acquisition of greater dexterity on the part of the intact limb

of the hemiplegic patient. These symptoms when present in full form are not always easy to detect. If present in a mild form, they may present themselves only as a disturbance in the ability to learn new tasks on the part of the intact upper extremity. Other symptoms which are said to be the result of parietal lobe lesions and which could disturb rehabilitation are loss of memory, disturbed attentiveness, and loss of abstract attitudes.

Another factor which can influence hemiplegic rehabilitation unfavorably is flaccidity. This condition usually is accompanied by severe motor disability. Although this was not a problem in the present series, it has been correlated with sensory loss[1,2] and related to lesions of the parietal cortex.[5–7,17] When flaccidity of the lower extremity exists in hemiplegia, ambulation is seriously disturbed.

There is some evidence for assuming that the lack of a good prognosis for rehabilitation in the presence of persistent sensory loss may depend simply on the size of the lesion present. Hemiplegia with additional sensory involvement indicates a posterior extension of the lesion. When the persistent sensory loss is both of a cortical and subcortical nature, then the lesion appears to be much larger. It is the latter category of patient which shows the worst prognosis. Lashley[16] has presented experimental evidence in support of the contention that the amount of tissue destroyed is the significant factor. He has quoted Jackson: "I would suggest (I cannot speak definitely) that if a small quantity of a nervous organ be destroyed, there is recovery; if a large quantity, there is some recovery; if of a very large quantity, scarcely any."

Ruch and co-workers[19] have offered evidence for the occurrence of return of sensory function as the result of retraining. They believed that retraining plays an important part in reducing the sensory deficit to a small permanent defect. Others have suggested that the return of function is largely a spontaneous process and is not dependent upon retraining.[9] The exact nature of this spontaneous process remains unknown. The term "diachisis" has been used to refer to the loss of function following cerebral insult which is spontaneously reversible. The present series offers evidence to support the contention that retraining does occur. How important this is in the return of function remains questionable. There were patients in this series exhibiting improvement in sensory function on both sides during the testing period. Most of these had lesions of recent origin, one and a half months or less. There were, however, some with much older lesions who revealed improvement bilaterally. Of the patients who showed improvement of the impaired side only, again most had disabilities of recent origin but there were some of much longer duration. Most patients who exhibited no improvement had had their disability three months or more. These data suggest that, since most improvement occurred during the first three months, the disability usually was in the nature of "diachisis." Those few cases which exhibited improvement, though the disability had been present for many months and years, suggest that retraining may play a significant role in return of function. It is doubtful in this series whether the actual testing situation could be the source of the retraining. All the patients were part of a rehabilitation program which included physical therapy, corrective therapy, and occupational ther-

apy where an effort was made to improve the dexterity of both upper extremities. It is probable that these activities were responsible for the improvement which occurred when the disability had been present for some time, as well as when the improvement occurred bilaterally.

CONCLUSIONS

In a series of 35 hemiplegic patients, evidence of persistent sensory loss could be correlated with a poor prognosis for rehabilitation and length of hospitalization. Eighty per cent of the patients revealed a disturbance of sensation. Vibratory sense, two-point discrimination, and pain sensation were all impaired in about equal frequency. Two-point discrimination returned to normal first (average one and a half months) and most often. Vibratory sense and pain sensation returned later (averages four and three-eighths months and two months, respectively) and about half as frequently as did two-point discrimination. Retraining was a factor in the return of sensory function with some patients.

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Ribosuria in Muscular Dystrophy

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CONFLICTING REPORTS have been made regarding the occurrence and significance of ribosuria in relation to muscular dystrophy and other diseases characterized by muscle wasting.[1-3] If ribose could be persistently recovered in the urine of patients with these diseases alone and not in the urine of normals, it is probable that the demonstration of ribosuria could be a valuable diagnostic tool in the discovery of early cases. It has been suggested by Orr and Minot[1] that the presence of ribose could indicate an error of general cellular metabolism. If substantiated, such a concept could further the understanding of the pathogenesis of these disorders. Therefore, an attempt has been made to establish the occurrence and persistence of ribosuria in a series of patients with muscular dystrophy.

SELECTION OF CASES

A diagnosis of muscular dystrophy was confirmed or established on clinical grounds in 45 patients whose ages ranged from four to 55 years. The majority (29) were 16 years or less in age; about one-third (16) were in the adult group, or over 16. Twenty-seven patients were found to have had a history of pseudohypertrophy of one or more muscle groups (table 1).

This group of patients can be subdivided according to the standard classification consisting of 1) the juvenile or Erb type, 2) the pseudohypertrophic or Duchenne type, and 3) the Landouzy-Dejerine or facioscapulohumeral type.[4] Our basis for classification was the presence or history of enlarged calf muscles, the age of onset of the dystrophy, and the distribution of muscular involvement. Many cases did not show the classically described characteristics of a specific form of muscular dystrophy, thus resulting in an extensive overlapping of classification. In eight of the 20 males there was a family history of the disease, suggesting a sex-linked recessive trait. A definite family history of dystrophy was found in 18 patients of this group. Some degree of pseudohypertrophy involving muscles other than the plantar flexors was present in two cases of juvenile dystrophy. Pseudohypertrophy also occurred in two patients with the facioscapulohumeral form of the disease. Careful examination of facial muscles resulted in detecting abnormalities in six patients who were classified in the pseudohypertrophic group.

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TABLE 1
DISTRIBUTION OF PATIENTS ACCORDING TO GROUP

	Male		*Female*	
	Under 16	*Over 16*	*Under 16*	*Over 16*
Pseudohypertrophy	17	3	1	2
Facioscapulohumeral	0	4	0	5
Juvenile or Erb's	9	1	3	0

Each patient had a complete physical examination in which general nutritional status and degree of skeletal deformity were noted. In addition to clinical examination of the cardiovascular system, an electrocardiogram was made in an effort to discover dystrophic involvement of the heart.[5–7] The presence and degree of atrophy or pseudohypertrophy of muscle groups were evaluated. In every patient the strength of muscle groups performing a certain function was measured on the basis of the ability of these muscles to perform against graduated degrees of resistance. Usually the proximal muscles of the limbs were the earliest and most severely involved. Absence of the knee jerks with preservation of ankle jerks was frequently observed. Many patients unable to elevate their upper extremities had relatively good strength in their forearms and hands.

TABLE 2
MUSCULAR DYSTROPHY PATIENTS

Subject	*Age*	*Type*	*Weight (kg.)*	*Obesity*	*Atrophy*	*Total creatine and creatinine C/kg.*	*Preformed creatinine C/kg.*	*Creatine C/kg.*	*Ribose mg./gm. total C*	*Ribose mg./gm. creatinine*
1. T.B.–male	3	Juv.	15.4	0	2+	29.9	10.7	19.2	5.8	24
2. R.K.–male	5	P.H.	22.7	0	2+	26.8	7.9	18.9	28.	95
3. C.L.–female	7	Juv.	36.4	1+	2+	18.3	5.1	13.2	25.4	95
4. S.S.–male	8	P.H.	27.2	0	1+	23.8	9.3	14	26.2	68
5. J.S.–male	9	P.H.	28.	0	2+	39.4	13.5	25.9	9.2	24.2
6. J.R.–male	9	P.H.	22.7	0	2+	27	8.9	18.1	14.3	43.6
7. D.H.–male	9	P.H.	26.4	0	2+	19.6	8.8	10.8	31	68.5
8. J.G.–male	11	Juv.	23.6	0	2+	39	10.1	28.9	23	82.0
9. J.McD.–male	10	P.H.	34.5	0	2+	29.3	8.6	20.7	15	42
10. J.K.–male	11	P.H.	50.4	1+	2+	17.2	4.8	12.4	26.6	95.5
11. J.R.–female	11	Juv.	47.	1+	1+	23.8	11.8	12	22.9	41.2
12. M.B.–male	11	P.H.	44.5	1+	2+	21.2	5.2	16	10.6	95.7
13. L.R.–male	11	P.H.	23.6	0	3+	24.8	8.0	16.8	15.6	48.4
14. F.N.–male	11	Juv.	32.3	0	3+	32.0	11.0	21	11.7	34.2
15. B.P.–male	12	P.H.			2+				25.0	100
16. L.W.–male	12	P.H.	43	0	2+	26.5	8.9	17.6	10.9	32.6
17. J.N.–male	12	P.H.	27.3	0	1+	30.8	8.5	22.8	18.9	65.5
18. A.D.–male	12	P.H.	43	0	3+	32.0	8.8	23.2	15.2	56.0
19. L.B.–male	12	Juv.	45.4	1+	2+	16.2	4.2	12.0	30.5	116.5
20. P.S.–male	13	Juv.	25.4	0	2+	36.5	9.6	27.5	24.6	100
21. T.K.–male	14	P.H.		0	1+	24.6	12.1	12.5	14.6	29.6
22. C.L.–male	15	Juv.	59	0	2+	20.5	3.5	17.0	10.7	61
23. D.B.–male	16	P.H.	38.6	0	3+	20	5.4	13.0	13.5	46
24. B.F.–male	21	P.H.	36.0	0	3+	32.5	8.2	24.3	22.2	58.2
25. R.K.–male	22	FSH	76	1+	1+	28	23.2	4.8	9.7	11.7
26. H.S.–female	23	FSH	42.6	0	1+	28.3	20	8.3	17.8	24.7
27. M.K.–female	26	FSH	61	1+	1+	22.3	13.1	9.2	9.5	16.4
28. D.S.–male	28	FSH	41	0	3+	39.8	13.3	26.5	14.1	42.5
29. H.G.–female	40	P.H.	50	0	1+	21.4	9.4	12	27.1	77.5
30. H.T.–female	55	FSH	80	1+	1+	11.9	8.8	3.0	19.0	35.0

Eight healthy adults and 13 hospitalized patients either awaiting elective surgery or recovering from relatively minor surgical procedures were used as controls. The age range of this group was four to 37 years. In most of the adults, eight-hour night specimens were used; otherwise, 24-hour specimens were collected. Thirty of the 45 patients with muscular dystrophy cooperated sufficiently well to provide 24- or 48-hour urine samples. These urines were collected in the homes of the patients without direct medical supervision. When there was evidence of inadequate collection, the specimens were discarded. However, most of the creatine and creatinine values on duplicate collections showed satisfactory agreement (table 2).

METHODS AND RESULTS

Since the use of osazones in identification of sugars is at best an ambiguous technic, it was decided to try to confirm the observations of Orr and Minot[1] with a more critical method. The paper chromatographic technics, as outlined by Jermyn and Isherwood,[8] were chosen (table 3). The non-aqueous phases of two different solvent systems were used: 1) acetic acid, ethyl acetate, and water (1-3-3), and 2) pyridine, ethyl acetate, and water (1-2-2). The sugars were identified by spraying the dried papers with a mixture of oxalic acid, alcohol, analine, and water.[9] Hexoses showed as brown spots and pentose as bright red spots after heating the dried paper for ten minutes at 100° (figure 1).

The initial experiments were carried out on toluene preserved urines. Urine samples were cleared of urea by treatment with urease. Precipitation of the urease and other troublesome substances was accomplished by mercuric sulfate in H_2SO_4, neutralized by barium carbonate, and final removal of remaining ions was accomplished by passing successively through IR4B and IR 120. The resulting solution was essentially electrolyte free and after evaporation of the water under reduced pressure was dissolved in methanol. In this way the sugars contained in 10 ml. of urine were concentrated to a volume of 1 ml. of methanol. The equivalent of 0.5 ml. to 1 ml. of urine was dried at the starting point of the chromatogram. The papers were equilibrated in jars saturated with the solvent for at least eight hours before starting. They were allowed to run 16 hours, a sufficient time to separate all the sugars. Ribose, the fastest moving sugar, was near the bottom of the paper. A preliminary examination of a number of urines from normal and dystrophy patients showed no trace of free ribose, though 10 gamma, when added to 20 ml. of urine, could just be identified while the addition of 50 gamma resulted in a well defined spot.

Four other substances reacting as sugar to analine in oxalic acid could be demonstrated. One in the same position

TABLE 3
RIBOSE GROUP

	Male		*Female*	
	Under 16	*Over 16*	*Under 16*	*Over 16*
Pseudohypertrophic	15	1	0	1
Facioscapulohumeral	0	1	0	4
Juvenile or Erb's	6	0	2	0

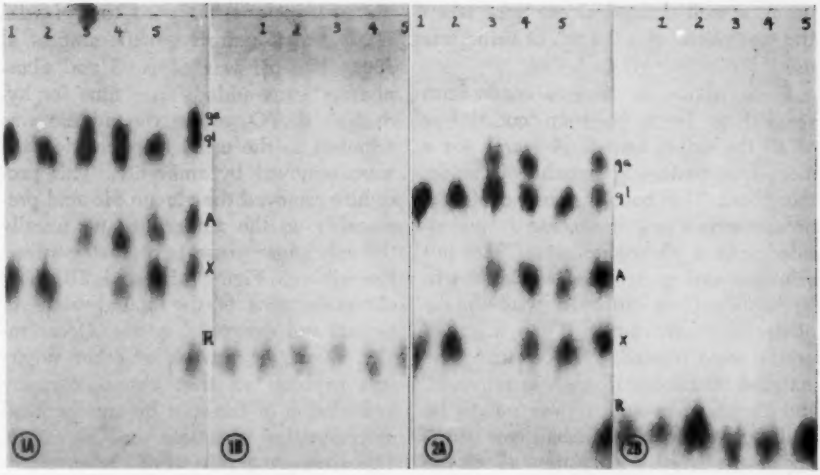

FIG. 1. Chromatograms of urinary sugars. Solvent: acetic acid, ethyl acetate, and water. 1, 2, normal urine; 3, 4, 5, muscular dystrophy urine. *A.* Free sugars. *B.* Bound ribose liberated by acid and phosphatase hydrolysis after elution from Norit. Lettered spots authentic sugars: gl. glucose; ga. galactose; A. arabinose; X. xylose; R. ribose.

FIG. 2. Chromatograms of urinary sugars. Solvent: pyridine, ethyl acetate, and water. 1, 2 normal urine; 3, 4, 5, muscular dystrophy urine. *A.* Free sugars. *B.* Bound ribose liberated by acid and phosphatase hydrolysis after elution from Norit. Lettered spots authentic sugars: gl. glucose; ga. galactose; A. arabinose; X. xylose; R. ribose.

on the chromatogram as glucose was present in all urines tested. Several showed another spot staining as hexose and in the position of galactose. This could best be demonstrated when the alkaline solvent was used. With the acid solvent, the two spots overlapped. Two other spots were usually present, both giving the red color of pentose with analine. They were in the same positions on the chromatogram as xylose and arabinose. These substances have not been further investigated, but it is known that these dietary pentoses may occur in the urine. In our experience, telling patients to refrain from eating fruit is not sufficient to eliminate these sugars from the urine. In any case, these sugars did not interfere with the identification of ribose by this procedure, and, therefore, such instructions were omitted for later collections. Samples of urine from 20 dystrophy patients were tested in this manner, as well as 10 normal urines. Free ribose was absent in all. Figures 1A and 2A show representative chromatograms of free sugars for normal and dystrophy urines.

Minot and Frank,[10] in later work, indicated the probable combined nature of the ribose in urine. Hydrolysis was used, therefore. Urines were heated one hour with normal H_2SO_4. The hydrolysates, after neutralization, were treated with urease, cleared with mercuric sulfate and barium carbonate, and salts removed with amberlite as for unhydrolyzed urine. Both normal and dystrophy urines tested showed, in addition to the spots obtained on unhydrolyzed

urine, a well defined ribose spot when the equivalent of a 0.5 ml. of urine was used.

Such ribose in a combined form seemed to be a common constituent of all the urines tested. A search for a more quantitative approach was made, therefore. The bound ribose could be present either as a nucleotide or nucleoside or as a phosphate ester. The nucleotides and nucleosides are known to be adsorbed on Norit A, while phosphate esters are not.[11] When acidified urines were treated with Norit A, the material containing ribose was removed, and therefore, would appear not to be a phosphate ester. By exhaustive washing of the Norit with water, all of the free sugar could be removed. Washing by centrifugation proved tedious, but could readily be accomplished with a column. Chromatographic tubes 1 cm. in diameter were used and a layer of charcoal 1 cm. in depth was sufficient to completely adsorb the ribose compound contained in 20 ml. of acidified urine. Washing with 200 ml. water completely removed free sugars, urea, and salts. The pigments of urine, purine compounds including uric acid, any pyrimidine compounds that might be present, and glucuronosides are retained by the Norit, as well as certain other materials such as phenolic compounds. These may be eluted with 50 ml. of ammonical acetone water (1-40-60). Since glucuronic acid derivatives are present along with the ribose containing compounds, a direct colorimetric determination was not possible. The following procedure was used therefore. The samples were evaporated to remove ammonia and acetone, adjusted to 1 N with H_2SO_4, and hydrolyzed 10 minutes at 100°. The pH was adjusted and phosphatase* was added; after time for hydrolysis of PO_4 esters, the protein was removed in the usual manner and salts were removed by amberlite. This procedure removed the glucuronic acid presumably on the amberlite, and usually the only sugar present chromatographed like ribose. Figures 1B and 2B show chromatograms of the bound sugar in normal and dystrophy urines. Occasionally, there were traces of other sugars still present, so that chromatography and elution of the spot before chemical determination of ribose was necessary. The chromatograms were run in triplicate, with a standard solution on one edge of the paper, and on the other edge, an enzyme blank (this occasionally contained traces of glucose). The paper was cut in strips and one stained along with the standard to locate the position of the ribose. The other two were eluted with water for duplicate sugars, and a like area in size and position from the final strip was used as a blank. The orcinal test was used.[13] Under these conditions, the blank was small but appreciable and was deducted from the reading for the sample. While no great accuracy is claimed for this procedure, 85 to 95 per cent of the ribose of adenylic-5-P could be recovered by this process, either alone or added to urine. This ester is the most difficult to hydrolyze of the purine esters. Ribose combined with a pyrimidine would not be hydrolyzed by this procedure. It was believed that the procedure was quantitative enough to reveal any great dif-

*The preparation of acid phosphatase was made from Polidase-S from the Schwartz Chemical Laboratories by the procedure of S. S. Cohen.[12] Purification was essential since the product contains glucose, which a final dialysis completely removed.

TABLE 4
NORMAL CONTROLS

Subject	*Age*	*Weight (kg.)*	*Total creatinine and creatine C/kg.*	*Preformed creatinine C/kg.*	*Creatine C/kg.*	*Hydrolyzable ribose mg./gm. total C*	*Hydrolyzable ribose mg./gm. creatinine*
1. T.K.–male	4	17.8	22.7	14.8	8.9	21.4	35.8
2. D.M.–female	7	21.1	28	21	7	18.5	24.2
3. R.S.–male	8	23.6	29	20.6	8.4	17.7	24.4
4. M.B.–female	9	24.9	19.2	16	3.2	17.3	20.7
5. E.S.–male	9	27.8	25.8	18	7.8	18.9	28
6. R.C.–male	11½	32.7	24.3	17.4	6.9	17.3	22.3
7. W.A.–male	12	34.2	23	19	4	13.4	18.7
8. J.B.–female	13	37.3	26.8	22.4	4.4	18.6	22.1
9. B.S.–female	13	48.2	22.1	16.6	5.5	11.3	16.5
10. L.M.–male	18	63.4	27	25.2	1.8	11.4	11.9
11. C.A.–male	20	68	21	20.6	0.4	11.65	11.9
12. C.L.–male	23	58	23.9	22	1.9	9.3	10.1
13. K.E.–male	24	93	25	21.4	3.6	9.9	10.8
14. S.M.H.–male	24	75	25.2	22.5	2.7	11.8	13.3
15. I.D.–male	25	79	25.6	23.9	1.7	11.9	12.8
16. B.E.–male	31	73	24.3	21.9	2.4	9.7	10.9
17. R.W.–male	29	94	24.7	23.9	0.8	9.7	10.2
18. T.C.–male	30	80	28.6	26	3.6	11.9	12.8
19. S.W.–male	31	66	24.5	22	2.5	13.9	14.9
20. A.M.–male	35	81.5	22.4	22	0.4	10	10
21. R.L.–male	37	75	25	24	1	9.6	10

ferences in the ribose content of urine of muscular dystrophy patients as compared with normals.

Table 2 shows the data for the total creatine excreted per kg. of body weight, and the preformed creatinine per kg. The ribose per gm. of preformed creatinine and of total creatinine plus creatine is also included. In columns 5 and 6, the extent of obesity and atrophy of muscles is indicated. It can be seen in confirmation of other workers[14–17] that, while the total creatine plus creatinine values are fairly constant and of the same order as in normals, shown in table 4, the excretion of preformed creatinine is low and variable. This would seem to indicate that the ability of the body to form creatine is normal and that not held in the muscle as phosphocreatine is excreted unchanged. The lowered creatinine is a reflection of the amount of degeneration having taken place in the muscle mass, and may be quite unrelated to the cause of the disturbance.

There are considerable variations in ribose excretion per gram of total creatine plus creatinine, both in normals and in muscular dystrophy patients. When the values are plotted on a scatter diagram against the age of the subject, there is a trend toward larger values in the younger age group in both controls and dystrophy cases, with the dystrophy

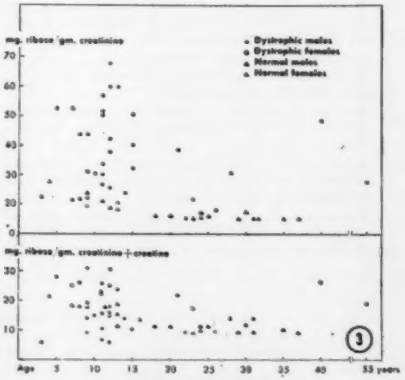

FIG. 3. Ribose content of urine.

cases tending to be about the same as the controls (figure 3).

If the main source of the ribose were from a substance like adenylic acid, which though present in all tissue is much more abundant in muscle, then it would be appropriate to plot values referred to preformed creatinine. Since the creatinine excretion tends to be low in muscular dystrophy, the difference between normals and patients becomes more impressive (figure 3). Whether these comparisons are justified will depend on the nature of the substances containing ribose and its probable source.

CONCLUSION

This investigation of ribose in urine does not confirm previous reports that ribosuria distinguished patients with muscular dystrophy from normal controls.

No free ribose was found in the urines of 20 of the dystrophy patients or in urines of ten of the control subjects.

Hydrolysis of the urines of both dystrophic and control subjects released small amounts of bound sugar. From the position on the chromatogram, the substance appears to be ribose.

Quantitative methods yielding approximately 85 per cent of known amounts of ribose from adenylic acid revealed no significant differences between patients with muscular dystrophy and normal controls.

No correlation was found between the amount of ribose and the clinical manifestations of the dystrophy.

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Mental Status of Children with Convulsive Disorders

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THE PURPOSE of the investigation reported in this paper was to determine the mental status of children with convulsive disorders, and to inquire into the possible relation of mental retardation to such factors as type of convulsive disorder, etiologic factors, age at onset of convulsive attacks, and the relation of the electroencephalographic findings to mental retardation and clinical diagnosis.

The medical records of 355 patients who were first examined in the section of pediatrics of the Mayo Clinic between November 1, 1950 and December 31, 1951, and whose condition was diagnosed as a convulsive disorder were examined. It was considered that a more representative group would be obtained if the variables which might be associated with return visits were excluded. Of the 355 histories examined, 43 were omitted from the study because they indicated that each patient had had only a single febrile convulsion accompanying some acute illness, and 16 were omitted because the clinical record was incomplete with respect to essential data. This study is based on the remaining 296 cases.

It shoud be stated that although all patients at the clinic are seen on a private basis, a wide range existed in the economic level of this group. Geographically, the study included children from 36 states and five countries. No effort was made to distinguish between those patients seen at the clinic on an outpatient basis and those who were hospitalized, inasmuch as there was frequently an overlap, some patients being seen at times at the clinic prior to hospitalization, at other times after hospitalization; others were seen only at the hospital or only at the clinic.

The children were rated in regard to intelligence level in three groups as 1) retarded, 2) dull-normal, and 3) average or better. The rating was made on the basis of either psychologic tests or the physicians' evaluation. The general practice in the section of pediatrics, in order to avoid unnecessary expense to the patient, is to request psychologic tests when 1) there is a question of

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TABLE 1
MENTAL STATUS OF 296 CHILDREN HAVING CONVULSIVE DISORDERS

Mental rating	Total No.	Total Per cent	Basis of rating: I.Q. test No.	I.Q. test Per cent	Basis of rating: Physician's estimate No.	Physician's estimate Per cent
Retarded	111	37.5	65	53.7	46	26.3
Dull-normal	43	14.5	31	25.6	12	6.9
Average or better	142	48.0	25	20.7	117	66.8
Total	296	100.0	121	100.0	175	100.0

mental retardation, 2) it is felt that the results of the tests will be of help in enabling the parents to accept the fact that their child is retarded, and 3) the diagnosis or clinical history is suggestive of mental deterioration. There were 175 children whose intelligence ratings were based on the physicians' evaluation; in the 121 remaining cases they were based on the results of the psychologic tests. The intelligence tests used were as follows: Revised Stanford–Binet Intelligence Scale (L) in 48 cases, Wechsler Intelligence Scale for Children in 27 cases, Wechsler–Bellevue Intelligence Scale in six cases, Cattell Infant Intelligence Scale in 38 cases, and the revised Vineland Social Maturity Scale in two cases.

The intelligence ratings are shown in table 1. It is seen that whereas 53.7 per cent of the children rated by psychologic tests were judged retarded, only 26.3 per cent of the group evaluated by the physicians were judged as retarded. Of the total group 37.5 per cent were considered to be retarded, 14.5 per cent dull-normal, and 48 per cent average or better. These proportions are in contrast with those of Wechsler[1] for a random normal population, who reported 9 per cent retarded, 16 per cent dull-normal, and 75 per cent average or better. Wechsler's group is not strictly comparable with the group we are reporting in that the age distribution of our group (two months to 14 years) is narrower than his. The comparison, however, indicates a larger percentage of retardation found in this group of convulsive children than is generally to be expected in a random group. On the other hand, the percentage of the group reported herein as retarded (37.5 per cent) is in agreement with the estimated proportion of retarded children of elementary school age found among children with convulsions by the New York Board of Education[2] (38 per cent). It is also in agreement with the number of slightly subnormal and subnormal patients (36 per cent) reported by Lennox[3] in a survey of 1,905 epileptic patients outside of institutions.

Of the 296 children included in the study, 166 or 56 per cent were boys, and 130 or 44 per cent were girls. Their ages ranged from two months to 14 years, the mean age being six years two months. The incidence of retardation is shown in table 2, that is, the percentage of boys and girls graded as retarded in relation to their ages. The percentage retarded is slightly greater for the girls (39.2 per cent) than for the boys (36.1 per cent), but the difference is small and does not seem significant. A greater incidence of retardation was indicated among the younger children when the group was subdivided into five-year age groups, the incidence of retardation being 53.1 per cent in the group up to 5

TABLE 2
INCIDENCE OF RETARDATION IN RELATION TO SEX AND AGE: 296 CHILDREN

Age, years	Total			Boys			Girls		
		Retarded			Retarded			Retarded	
	Cases	No.	Per cent	Cases	No.	Per cent	Cases	No.	Per cent
0 to 5	147	78	53.1	83	45	54.2	64	33	51.6
6 to 10	75	18	24.0	40	11	27.5	35	7	20.0
11 to 15	74	15	20.3	43	4	9.3	31	11	35.5
Total	296	111	37.5	166	60	36.1	130	51	39.2

years of age, 24 per cent in the group 6 to 10 years of age, and 20.3 per cent in the group 11 to 15 years.

DIAGNOSIS AND RETARDATION

The children were subdivided according to diagnostic classification as petit mal, grand mal, mixed petit and grand mal, and other convulsive disorders. Each classification also is subdivided depending on whether the etiologic factors were definitely symptomatic or idiopathic as judged from the history and examination. If a diagnosis of symptomatic convulsive disorder was made, evidence of a definite demonstrable lesion such as hydrocephalus, hemiplegia, spastic cerebral palsy, porencephalia, or tuberous sclerosis was required. In cases of doubtful diagnoses, neurologic examinations and pneumoencephalograms were used to indicate gross neurologic lesions. Table 3 shows the percentage of retardation for these subclassifications. The total percentage of retardation among the diagnostic groupings is not great, none of them departing very much from the average for the group of 37.5 per cent. On the other hand, a striking and large difference exists between each group in which the etiologic factors were considered to be definitely symptomatic and those in which they were idiopathic. In the group with definite symptomatic evidence, the percentage retarded was 73 in contrast with 22.2 per cent retarded in the idiopathic group. As can be noted, the larger percentage of retardation in the symptomatic group is shown not only for the total group of symptomatic cases as compared with the total idiopathic group, but in each diagnostic subclassification.

AGE AT ONSET

It has been noted previously (table 2) that the frequency of retardation is greater among the younger children than among the older. In that analysis, age referred to age at time of diagnosis of the convulsions. Of greater interest, perhaps, is the relation of degree of re-

TABLE 3
DIAGNOSIS ETIOLOGIC DISORDER AND RETARDATION: 296 CHILDREN

Diagnosis	Total			Etiologic disorder					
				Idiopathic			Symptomatic		
		Retarded			Retarded			Retarded	
	Cases	No.	Per cent	Cases	No.	Per cent	Cases	No.	Per cent
Petit mal	62	22	35.5	45	11	24.4	17	11	64.7
Grand mal	125	50	40.0	90	20	22.2	35	30	85.7
Mixed	56	17	30.4	46	11	23.9	10	6	60.0
Other	53	22	41.5	26	4	15.4	27	18	66.7
Total	296	111	37.5	207	46	22.2	89	65	73.0

TABLE 4
RETARDATION AND AGE AT ONSET: 296 CHILDREN

Age at onset	Total			Etiologic disorder					
				Idiopathic			Symptomatic		
	Cases	Retarded No.	Retarded Per cent	Cases	Retarded No.	Retarded Per cent	Cases	Retarded No.	Retarded Per cent
Less than 6 mos.	49	32	65.3	22	9	40.9	27	23	85.2
6 mos. to 2 yrs.	83	41	49.4	47	14	30.0	36	27	75.0
2 yrs. 1 mo. to 4 yrs.	61	21	34.4	50	14	28.0	11	7	63.6
4 yrs. 1 mo. to 7 yrs.	37	8	21.6	31	3	9.7	6	5	83.3
7 yrs. 1 mo. to 15 yrs.	65	8	12.3	57	6	10.5	8	2	25.0
Not stated	1	1	–	0	0	–	1	1	–
Total	296	111	37.5	207	46	22.2	89	65	73.0

tardation to age of onset of the disease. In the analysis of age at onset in relation to retardation, it is to be kept in mind that etiologic aspects, in the sense of whether the convulsions were considered to be of symptomatic or idiopathic origin, were definitely related to retardation, and patients with symptomatic lesions showed a definitely higher incidence of retardation. In order to demonstrate the relation between age of onset and mental retardation the data were analyzed for the entire group and then separately for the idiopathic and symptomatic groups (table 4). In the total group, a very regular decrease in the per cent of retardation occurred with increasing age of onset. This is shown also in the idiopathic and the symptomatic groups, although in each group, probably because of the small numbers involved in some of the age groups, the regularity of the indicated relationship is somewhat disturbed.

FREQUENCY OF CONVULSIVE ATTACKS

A consideration that prompts attention is whether frequency of attacks, as an indication of the severity of the disease, is related to retardation. A rating was devised whereby the cases were classified in respect to frequency of attacks as 1) infrequent, 2) frequent, and 3) very frequent. The patient's history was studied and an attempt was made to estimate the frequency of attacks previous to any medication. In many cases, attacks had continued in spite of medication. It is realized that this method may not be entirely satisfactory, but it did permit grouping within a considerable but definite range. These ratings were related to the diagnostic classification as follows:

Infrequent attacks:
Petit mal – less than two seizures a week
Grand mal – not more than one seizure a month
Other – not more than one seizure a month

Frequent attacks:
Petit mal – varying from two seizures a week to ten a day
Grand mal – varying from two to ten seizures a month
Other – varying from two seizures a month to one a day

Very frequent attacks:
Petit mal – more than 11 seizures a day
Grand mal–more than 11 seizures a month
Other – more than one a day

Table 5 shows the incidence of retardation in relation to frequency of convulsive attacks. The percentage incidence of retardation is greater in the groups with more frequent attacks, a regular increasing progression being shown in percentage retardation as the groups with infrequent, frequent, and very frequent attacks are considered. It should be noted that this relationship is clearly shown not only in the total

TABLE 5

RELATION OF RETARDATION TO FREQUENCY OF CONVULSIVE ATTACKS: 288 CASES*

Frequency of attacks†	Total			Etiology idiopathic			Etiology organic		
	Cases	Retarded No.	Retarded Per cent	Cases	Retarded No.	Retarded Per cent	Cases	Retarded No.	Retarded Per cent
Infrequent	113	22	19.5	90	11	12.2	23	11	47.8
Frequent	102	41	40.2	69	17	24.6	33	24	72.7
Very frequent	73	42	57.5	45	16	35.6	28	26	92.9

*In 8 cases the frequency was not available from the clinic history.
†See text for definition.

group but also in the idiopathic and the symptomatic groups.

A considerable amount of research in the past has been interpreted as indicating that mental deterioration accompanies long-standing convulsive disorders. We attempted to determine whether our records would give any indication in this regard. Since this is a study of children we do not have a real measurement of the effect of a long-standing convulsive disorder on mental deterioration and we are of the opinion that longitudinal studies will be necessary to clarify this.

RETARDATION IN RELATION TO THE ELECTROENCEPHALOGRAM

It is of interest to know whether there is any relation between the diagnosis of mental retardation and the degree of abnormality indicated in the electroencephalogram. Electroencephalographic tracings were made for 283 of the 296 patients. The classification of these tracings in use in our laboratory is supplied by the electroencephalographic laboratory at the clinic and is as follows:

Delta rhythm.—This rhythm is characterized by random slow waves (0.5 to 4 per second) which are arrhythmic and nonrepetitive and usually are unaffected by eye opening and hyperventilation. Grading is as follows: grade 1, amplitude up to 30 microvolts; grade 2, amplitude between 30 and 60 microvolts; and grade 3, amplitude more than 60 microvolts.

Waves also are categorized as focal or generalized. For these statistics bilateral delta waves are classified as generalized.

Dysrhythmia.—This includes a general category of waves that are usually rhythmic and repetitive and that tend to be inhibited by eye opening and accentuated by hyperventilation. Also included in this category are specific forms of waves. The following grades are used: grade 1, minimal abnormalities, continuous or paroxysmal, with amplitude up to 30 microvolts; grade 2, moderate abnormalities, continuous or paroxysmal, with amplitude up to 60 microvolts; and grade 3, specific forms of waves, for example, spikes and sharp waves. The waves also are categorized as diffuse or focal.

Asymmetry.—This is an amplitude asymmetry of the alpha rhythm greater than 25 per cent.

Delta-dysrhythmia.—Records show mixtures of delta rhythm and dysrhythmia. To maintain simplicity these cases have not been graded but are considered as a single mixed group.

The incidence of retardation among patients having idiopathic etiologic factors with normal electroencephalographic tracings or dysrhythmia, grade 1, is comparable to that of an average population (table 6). Among the patients with dysrhythmia, grades 2 and 3, and focal dysrhythmia, grade 3, the incidence of retardation definitely increases. In the group having symptomatic etiologic factors the incidence of retardation is uniformly high regardless of the electroencephalographic findings. In ten cases delta waves were present in the tracings, but they were so few in number that we did not consider them.

It was possible to relate the clinical diagnosis, that is, the type of attack, of

TABLE 6

RETARDATION IN RELATION TO ELECTROENCEPHALOGRAPHIC TRACINGS: 273 PATIENTS*

Electroencephalographic tracing	Etiologic Disorder					
	Idiopathic			Symptomatic		
		Retarded			Retarded	
	Cases	No.	Per cent	Cases	No.	Per cent
Normal	25	1	4.0	10	8	80.0
Dysrhythmia, grade 1	29	3	10.3	7	5	71.4
Dysrhythmia, grade 2	45	11	24.4	14	8	57.1
Dysrhythmia, grade 3	83	22	26.5	33	28	84.8
Focal dysrhythmia, grade 3	18	4	22.2	9	4	44.4

*Electroencephalographic tracings were made for 283 of the 296 patients. In 10 cases the tracings did not present adequate information for this classification.

283 patients to the electroencephalogram (table 7).

The electroencephalograms of 35 patients, or 12.4 per cent of the 283 patients, were considered normal, although the patients had convulsive attacks. If we include in this group those patients who had dysrhythmia, grade 1, the number of cases is 71 or 25.1 per cent.

Our study did not show any specific type of electroencephalographic tracing to be characteristic of any one clinical type of convulsive disorder. Dysrhythmia, grade 3, which shows a hump and spike (dart and dome) tracing, occurred commonly in cases in which the clinical diagnosis was petit mal (55 per cent), but it also occurred slightly more commonly in the cases in which the diagnosis was the mixed type (58.9 per cent).

SUMMARY AND CONCLUSIONS

Two hundred and ninety-six children with a diagnosis of convulsive disorders were rated as to mental retardation in three groups: 1) retarded, 2) dull-normal, and 3) average or better. The rating was accomplished on the basis of the clinician's evaluation or on the results of psychologic testing, if the former was considered inadequate. The findings indicated that the group as a whole showed a larger incidence of retardation (37 per cent) than a general normal group (about 10 per cent). The percentage of retardation was greater in cases of convulsive disorders diagnosed as definitely symptomatic (73 per cent) than in those classified as idiopathic (22.2 per cent).

The younger children in the group showed a greater incidence of retardation than the older children. It also was found that the incidence of retardation was greater among the patients who had more frequent convulsive attacks than

TABLE 7

DIAGNOSIS IN RELATION TO ELECTROENCEPHALOGRAPHIC TRACINGS: 283 CASES*

Electroencephalographic tracing	Diagnosis							
	Petit mal		Grand mal		Mixed		Other	
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
Normal	10	16.7	17	14.7	4	7.1	4	7.8
Dysrhythmia, grade 1	4	6.7	18	15.5	6	10.7	8	15.7
Dysrhythmia, grade 2	11	18.3	26	22.4	10	17.9	12	23.5
Dysrhythmia, grade 3	33	55.0	38	32.7	33	58.9	12	23.5
Focal dysrhythmia, grade 3	2	3.3	13	11.2	3	5.4	9	17.7
Other	–	–	4	3.5	–	–	6	11.8
Total	60	100.0	116	100.0	56	100.0	51	100.0

*Electroencephalographic tracings not made for 13 patients.

among those who had less frequent attacks.

No relation was found between the incidence of retardation and the diagnostic classification of petit and grand mal. Patients with dysrhythmia, grades 2 or 3, or focal dysrhythmia, grade 3, showed a definite increase of incidence of mental retardation as compared to those with normal tracings or dysrhythmia, grade 1. Among patients with symptomatic convulsive disorder the incidence of retardation was high, regardless of the electroencephalographic findings.

Of the patients with convulsive disorder, 12.4 per cent had normal electroencephalographic tracings. On the basis of the findings in this study no specific type of electroencephalographic tracing appeared characteristic of any one clinical type of convulsive disorder.

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■ Professor Matteucci, nearly twenty years ago, found that when a nerve going to a muscle is put upon another muscle, a contraction takes place in the first one when the second contracts. In this case the nerve receives an *excitation* at the time the muscle, upon which it lies, contracts. The cause of the excitation of the nerve, according to Professor Matteucci, is a galvanic discharge which accompanies the muscular contraction. Dubois-Reymond explains otherwise the excitation of the nerve. He thinks it is due to a diminution of the galvanic current of the muscle when it contracts, and that the changes occurring, in consequence, in the nerve irritate it. But whatever be the right explanation, it seems certain that it is *some change in the galvanic state* of the muscle which causes the excitation of the nerve. We will, therefore, call it a galvanic excitation. Now, I have tried to prove, in 1849, that the sensitive nerve-fibres which are in muscles, receive that peculiar galvanic excitation which acts upon the motor nerves in the case of the precipitation which acts upon the motor nerves in the case of the preceding experiment, so that there is a galvanic cause of sensation in muscular contractions.

C. E. Brown-Sequard in *Lectures on the Physiology and Pathology of the Central Nervous System*, published in 1860.

CLINICAL PATHOLOGIC CONFERENCE

E. P. Richardson, Jr., M.D. Section Editor

Presented by *Gilberto Gamez, M.D., Ephraim Roseman, M.D., Gerald M. Peterson, M.D. and Ludwig H. Segerberg, M.D.*

PRESENTATION OF CASE

A 44 year old white widow was admitted to the hospital on July 10, 1951 with complaints of pain in the right lower abdomen since 1936 and difficulty in walking since 1949.

The patient dated the onset of her present illness to approximately 1936. At that time her husband suddenly died of heart disease and she was quite upset. Shortly after his funeral she noted pain in the right lower quadrant of her abdomen for the first time. This pain radiated down to the right side of the vagina, and was described as mild and rather like a toothache in character. It was intermittent and disappeared for periods as long as several weeks. This pain became worse when she became upset or nervous or excited. It ws not affected by coughing, straining, or sneezing. At times the pain seemed to originate under the right costal margin at the level of the midaxillary line. There had been no change in the character of the pain over the 15-year period, and at no time had she had any pain on the left side of her body. Early in 1949 she noticed that she began to limp. This limp involved the right lower extremity and became slowly but progressively worse so that she had increasing difficulty in walking. The limp apparently was due to weakness of this extremity. She had had no numbness or paresthesias. It was stated that both legs frequently felt cold. Six months prior to admission she had had intermittent pain in both calves associated only with fatigue.

The past history revealed that she had always been in good health and had had no serious illnesses. There was no history of headaches, visual disturbances, backache, or sphincter difficulties. She had been constipated all of her life. The remainder of the past and family histories was non-contributory.

Physical examination: The patient was a well developed, well nourished white female who did not appear to be ill. She was alert and cooperative. Her temperature was 98.8°. Blood pressure was 135/90. Pulse rate was 84 and respirations 22 per minute. There was no evidence of lymphadenopathy. The heart was normal in size and configuration. There were no abnormal valve sounds and no murmurs were heard. The lung fields were clear. The abdomen was soft and there were no abnormal palpable masses. There was no tenderness or rigidity.

She was able to appreciate the odor of ground coffee readily in both nostrils. Visual fields were full to confrontation. Visual acuity was 20/20 in both eyes. The fundi showed that both optic disks were distinct, there were good cups bilaterally, and the vessels were normal. There was no evidence of hemorrhages, exudates, or abnormal pigmentations. The right pupil measured 4 mm., and the left 3 mm. Both pupils reacted briskly to flashlight and through a good range. The extraocular movements were normal. There was no nystagmus. The corneal reflexes were equal and active bilaterally. Sensation on the face to cotton and pinprick was normal. Strength and tone of the masseter and temporal muscles on both sides were normal and equal. There was no evidence of any facial weakness. Air conduction was greater than bone conduction bilat-

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erally, and the Weber test was not referred. Hearing was considered to be normal. Speech was not remarkable. The uvula elevated in the midline. The gag reflex was equal and active bilaterally. The tongue protruded in the midline and there was no evidence of any atrophy or fibrillation.

The patient walked with a limp favoring the right lower extremity, and her walk could be described as a "tight" one, in which she took small steps and appeared to be quite stiff. With her eyes closed she tended to fall to the right on carrying out the Romberg maneuver. On walking with her eyes closed, she tended to fall to the right.

There was no tenderness or limitation of motion of the spine.

The motor system revealed that there was no evidence of any wasting, weakness, or abnormalities of tone in the upper extremities. Using the dynamometer she was able to squeeze 40 kg. on the right and 30 kg. on the left. The patient was right-handed. There was a moderate amount of weakness in both lower extremities. The degree of weakness in the right lower extremity was estimated about 50 per cent and that in the left lower at 25 per cent. The left calf measured 30.5 cm. and the right 28 cm. The left thigh just above the patella measured 33.5 cm. and the right 33 cm. Resistance to passive manipulations was moderately increased in both lower extremities, particularly on the right side. No fibrillations were seen in the lower extremities. Stretch reflexes in the upper extremities were normal and equally active. In the lower extremities all the reflexes were hyperactive, particularly those on the right side. There was unsustained ankle clonus bilaterally. There was a bilateral plantar extensor response on plantar stimulation. There was a bilateral Strümpell sign. Only the left upper abdominal skin reflexes could be obtained. The lower abdominal musculature was weak and had poor tone. Examination to pinprick revealed a vague indefinite hypalgesia in the left lower extremity. Vibration sense was completely absent in both lower extremities, extending upward to the level of the third lumbar spine. She made numerous mistakes in the sense of position and in figure writing of both feet.

All tests for coordination were well carried out in the upper extremities. Upon doing the heel-to-knee test there was a marked amount of past pointing, terminal tremor, and ataxia, particularly with the eyes closed.

Laboratory findings: Urinalysis on July 11, 1951 showed a specific gravity of 1.003, with a pH of 5.5. There was a negative reaction for albumin and sugar. There were no abnormal microscopic elements. Blood count on July 11 showed 4.34 million red blood cells and 3,850 white blood cells per cu. mm. There were 60 per cent neutrophils, 2 per cent eosinophils, 4 per cent monocytes, and 34 per cent lymphocytes. The hemoglobin was 13 gm. The blood and cerebrospinal fluid Wassermann reactions were negative.

Lumbar puncture was done on July 11, 1951 and the initial pressure was 180 mm. of water. The dynamics were described as normal. The fluid contained no cells, two plus globulin, and total protein of 220 mg. per cent. The gold curve was 0000012110.

An electroencephalogram on July 12, 1951 was a moderately dysrhythmic one but showed no evidence of any focal expanding intracranial lesion. Roentgenograms of the skull revealed that there were no abnormalities of the vault or evidence of any bone destruction. The sella turcica was normal. The pineal gland was not calcified. There was a symmetrical calcification in the glomus of the choroid plexus on either side, but there was no evidence of displacement.

A pneumoencephalogram on July 13, 1951 revealed that the ventricular system and basilar cisterns were well filled. There was no displacement in the ventricular system, but the left lateral ventricle was slightly larger than that on the right. The basilar cisterns, as well as the cerebral sulci, were normal in appearance.

DISCUSSION

DR. GILBERTO GAMEZ (fellow in neurology): We shall attempt to analyze the available historical data to see if we can from the history alone arrive at an anatomic location of the lesion. We have a woman who at the rather early age of 29 (1936), following some emotional trauma, developed for the first time a mild pain in the right lower quadrant radiating down the right side of the vagina. On careful consideration, this indicates that this is the pattern of distribution of the ilio-inguinal nerve, derived chiefly from the first lumbar segment. In about 50 per cent of individuals, the last thoracic nerve contributes fibers to this nerve. We mention this because the pain is said to originate at times from the right costal margin, which may mean involvement of higher nerves. Pain being the only complaint at this time, we may pos-

tulate that only sensory fibers were affected. Thus we could trace the fibers back to where they are not mixed with motor fibers, that is, to the dorsal root of the spinal nerve. There are some peculiarities of this pain such as intermittency (being absent as long as several weeks), and that it was not affected by coughing, sneezing, straining, or changes in posture. This latter would seem to point against compression on a root. For the next 13 years, nothing of particular significance happened. Then, in 1949, the patient, now aged 42, developed what could be interpreted either as a new symptom of the same disorder or an entirely different entity, manifested by slowly progressive weakness of the right lower extremity. I would like to mention at this point that the walking difficulty was probably more marked in the dark or when she closed her eyes, due to posterior column involvement. Also the weakness was probably not limited to the right lower extremity, but also involved the left to a certain extent. From its description we feel that this is a generalized weakness of the limbs rather than weakness of certain individual muscle groups. We would not like to incriminate the ventral spinal roots of the lumbosacral plexus. Rather this weakness indicates involvement of the pyramidal tracts, at least above the segmental innervation of the muscles of the lower extremities—that is, above L1 segment. There are no other sensory disturbances noted in the history except for the frequent sensation of coldness in both legs, which could probably be interpreted in different ways depending upon the accuracy of observation and verbalization of the patient. I would be inclined to interpret this symptom as occasional abnormalities of peripheral circulation.

About January or February 1951 (two years later) intermittent pain in the calf muscles seemed to be brought on by fatigue; again a possible explanation would be a circulatory disturbance. There is nothing in the past history of significant relationship to the present illness, except the negative information regarding back pain which leads one away from a possible vertebral column pathology.

Summarizing the history, then, we have a long drawn-out illness initially manifested by intermittent pain probably due to irritation of the dorsal spinal root of L1 or T12. Thirteen years later motor disability occurred (mainly on the same side), possibly due to involvement of the lateral pyramidal tracts at about the same level—L1 or T12. Considering the physical findings in the order of their relationship to the historical data, we note a severe motor disability of both lower extremities, particularly on the right, with about 50 per cent weakness. The tight and stiff gait, the moderately increased resistance to passive manipulations in the lower extremities, the hyperactive tendon reflexes with unsustained ankle clonus bilaterally, and the presence of pathologic reflexes all confirm our suspicion from the history for the involvement of the pyramidal pathways. The abdominal reflexes are a bit intriguing to explain. Although the abdominal reflexes probably utilize a short spinal reflex arc, they are normally dependent (for a reason not fully understood) upon the integrity of the pyramidal tracts, hence their absence could be interpreted in two ways: namely, pyramidal tract interruption above their reflex arcs, or direct interruption of their reflex arcs. The arcs of the abdominal reflexes are located in the spinal cord from T7 to T12. The upper abdominal reflex arcs are located at the levels of T7-9. Lesions at these levels cause disappearance of the reflexes. The presence of the left upper abdominal reflex denotes integrity of its arc above T9 or T10. The weakness and poor tone of the lower abdominal musculature is of further related significance. The lower halves of these muscles derive their innervation from the ninth and tenth thoracic segments of the cord, hence paralysis of these would put the lesion not lower than T9. We have thus established the level of the lesion to T9 or perhaps a segment above on the right and one or two segments lower

on the left. Let us now consider the level of the other pathways that are involved. Vibration sense was completely absent in both lower extremities up to the level of the third lumbar spine. This would correspond roughly to L1 segment of the cord, or maybe T12. Ataxia, terminal tremor, and past pointing brought about by closing of the eyes are further proof of involvement of the posterior columns. Both position and vibration senses follow the same pathway for conscious proprioception and their level of involvement in this instance would be the same, at approximately T12.

I would discount the vague hypalgesia in the left lower extremity because I suspect the patient is not a very reliable witness. However, if pressed for a possible anatomic explanation, I would suspect (though it is probably remote) the possible involvement of the lateral spinothalamic tract on the right side of the cord. There is a significant difference in the volume of the calf muscles, the right being smaller by 2.5 cm. I am not sure about the exact interpretation of this. It could be due to several possibilities: an atrophy of disuse, or anterior horn cell death at L4-5, or degeneration of peripheral nerves supplying these muscles. The first is a more tempting and logical explanation.

Recapitulating the anatomic distribution of the lesion, we have a disease affecting mainly the posterior and lateral columns of the cord on both sides. The higher level of pathology affects the lateral pyramidal tract up to T9 or a segment higher on the right. That on the left is a segment or two lower. The posterior columns of Goll and Burdach are involved up to the level of T11 or T12. Is this lesion, which seems to extend vertically from T9 down to L1 (or reverse) and involving mainly the lateral and posterior columns, intramedullary? From both the history and physical examination, it is quite difficult to make such a decision. If we go back again to the history, the earliest complaint being pain, we would be inclined to consider an extramedullary lesion as most likely. We would expect that it had grown around the dorsal root of L1 or T12 and over a course of 13 years gradually extended upward, and subsequently by expansion started pressing upon the cord posteriorly. Because the pain remained practically the same, the mass, whatever it was, must have avoided compressing the dorsal root but grew out of it upward along the subdural space. X-rays of the spine may or may not be of help in locating the lesion.

A lumbar puncture with carefully done manometric studies for the detection of a block would be valuable. On July 11, 1951 this was done and dynamics were described as normal. Taking this information at its face value we may presume the absence of a block. Merritt and Fremont-Smith[1] state that the "occurrence of normal dynamics in proved cases of cord tumor is so rare that the diagnosis is seldom justified unless block can be demonstrated." They give only one exception – that is, if the tumor is in the cauda equina, below the site of lumbar puncture. The normal initial pressure here is of no significance, for normal pressures or even lower ones are quite commonly found even in the presence of a block. More interesting and valuable information would be the final pressure after about 10 cc. of cerebrospinal fluid was drawn off, for a precipitous drop to more than 50 per cent of the original pressure may give us a clue. In contrast to the normal dynamics, we find a marked elevation of protein, a finding more in consonance with a subarachnoid block caused by an extramedullary lesion than that commonly found in intramedullary processes. At this point I am more undecided as to whether this is an intra- or extramedullary disease of the cord. A myelogram would be my final help. Etiologically there are a number of diseases which may present some of the salient features of this case. We shall mention some of those we thought about but discuss only those which are close to the present case.

Among the extramedullary, extradural diseases, we can easily eliminate disease

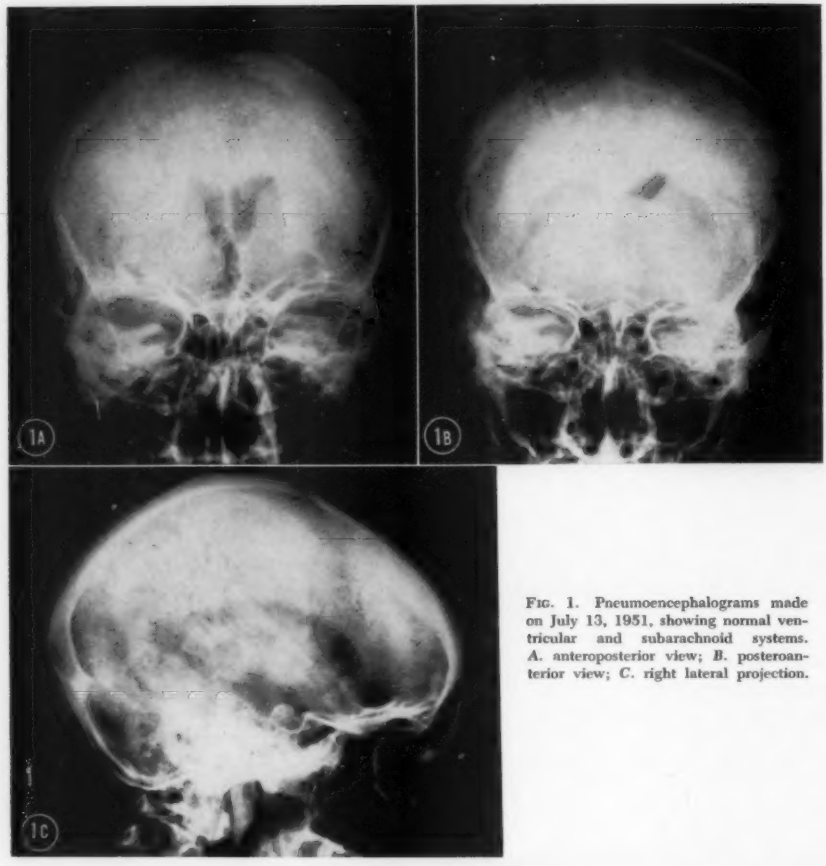

FIG. 1. Pneumoencephalograms made on July 13, 1951, showing normal ventricular and subarachnoid systems. *A*. anteroposterior view; *B*. posteroanterior view; *C*. right lateral projection.

of the vertebral column causing compression, such as Pott's disease and neoplasms of the vertebral bodies. This is an uncommon location for a herniated nucleus pulposus and we have no evidence to support it. Extradural abscess seems remote. It would be expected that in all diseases of the spinal column mentioned, pain would be made worse with posture and the course would be a more rapid one. Among the extramedullary, intradural possibilities, two slowly growing neoplasms must be given very careful consideration, namely meningioma and neurofibroma. These are the two commonest extramedullary tumors of the spinal canal and are most frequently found in the thoracic region. Of these two, the more likely would be the nerve sheath tumor for several reasons: 1) history of a root pain as the initial symptom; 2) these are most frequently seen in persons between 25 and 50 years, whereas meningiomas are common in the fourth and fifth decades of life; and 3) they commonly arise from tho-

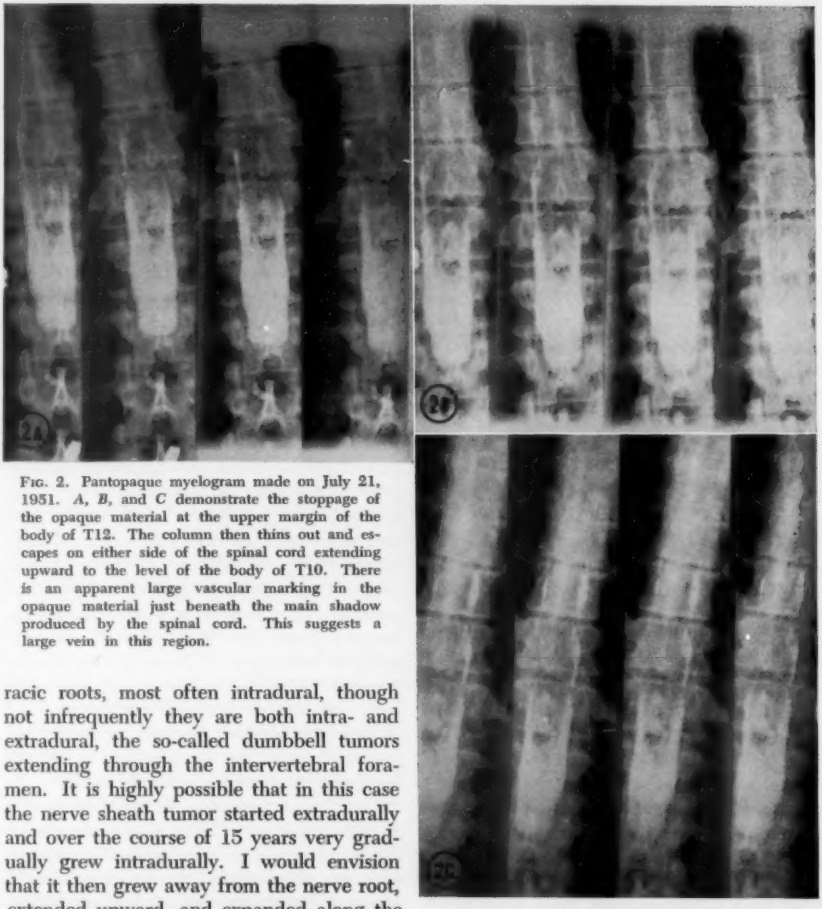

FIG. 2. Pantopaque myelogram made on July 21, 1951. *A, B,* and *C* demonstrate the stoppage of the opaque material at the upper margin of the body of T12. The column then thins out and escapes on either side of the spinal cord extending upward to the level of the body of T10. There is an apparent large vascular marking in the opaque material just beneath the main shadow produced by the spinal cord. This suggests a large vein in this region.

racic roots, most often intradural, though not infrequently they are both intra- and extradural, the so-called dumbbell tumors extending through the intervertebral foramen. It is highly possible that in this case the nerve sheath tumor started extradurally and over the course of 15 years very gradually grew intradurally. I would envision that it then grew away from the nerve root, extended upward, and expanded along the posterior wall of the spinal canal compressing only the dorsal and lateral columns, more partciularly the right.

Another extramedullary condition worth mentioning here, though quite rare, would be vascular anomalies of veins, such as varices, and arteries. This condition often produces a type of myelopathy which has been divided into two clinical forms. The condition is often diagnosed as thromboangiitis obliterans. Diagnosis is extremely difficult on clinical grounds. There are two forms: 1) The diffuse form is frequent in males of middle age. The onset is generally with pains preceding paraplegia. There is a succession of spastic to flaccid paraplegia with disappearance of the deep tendon reflexes and dissociated sensory loss. 2) The other type which more closely simulates this case is the localized form. This has a similar onset with pain and demonstrates recurrent neurologic signs. The picture is

of a nonspecific spastic "transverse myelitis."

Among the intramedullary diseases we mention neurosyphilis, particularly the tabetic form because of the posterior column involvement. However, there are many factors against this condition. We would expect decreased deep tendon reflexes. Above all the serologic tests on the blood and cerebrospinal fluid do not bear this out. In addition the fluid did not show cells. Among the degenerative diseases Friedreich's ataxia is probably closest because of the posterior and lateral column involvement. However, we would not find such a high protein in the cerebrospinal fluid. Syringomyelia has been mentioned as causing subarachnoid block. This occurs only when the cord has expanded, and then we might expect a very high protein value. However, this condition affects the upper cervical cord most often and by now we would expect dissociated sensory loss. The present case does not seem to give us the usual symmetric motor and sensory difficulty found in the so-called polyneuritis syndrome associated with collagen diseases. We would have more signs of peripheral nerve involvement.

Also among the intramedullary diseases is the condition called combined system disease or subacute combined degeneration of the cord generally associated with pernicious anemia. However, it may be due to other nutritional disorders. We have no evidence to support pernicious anemia and again we would not be able to explain the tremendous cerebrospinal fluid protein. I am almost tempted to say that this is an unusual type of multiple sclerosis limiting itself only to the spinal cord, the so-called spinal form, but this is a poor diagnosis and I would resort to it only after I had been reassured that this patient has no treatable disease. Except for the high protein it would be easy to explain all the symptoms on the basis of multiple sclerosis. So, to terminate, I would consider a benign slowly growing tumor arising from the nerve sheath of the dorsal root of L1 or T12, probably starting as an extradural one creeping inward, then upward along the spinal canal, dissociating itself subsequently from the root, pressing on the posterior lateral aspect of the cord particularly on the right side up to about the level of T9 or 8. This would be the so-called dumbbell type of schwannoma. This would be my first choice. My second would be multiple sclerosis.

DR. EPHRAIM ROSEMAN (neurologist): I should like to commend Dr. Gamez on his very excellent discussion, particularly his dissection of the history in order to make an anatomic localization and subsequently his use of the physical findings to confirm his original conclusions. There are several points which have been made and which should be emphasized. The fact that the patient did have root pain for some 15 years prior to the onset of paraparesis would certainly indicate a "benign" lesion. The fact that there was no more evidence of root compression, by way of continued pain, would tend to rule out diseases of the spinal column. In these, pain should invariably become worse on postural changes and particularly with any mechanism that would increase intraspinal pressure such as coughing, sneezing, or straining. A long period of root pain without evidence of cord compression would further decrease the likelihood of spinal column disease.

Yet, I feel that there is possibly a clue in the presence of the long intermittent history of root pain as to what the ultimate etiologic diagnosis might be. This would seem to point against an extramedullary tumor such as a neurinoma or meningioma, since it would seem hardly likely that 15 years could go by without the production of other symptoms. Furthermore, both of these two tumors might be expected to produce an exacerbation of pain particularly after five or ten years (and especially after evidence of cord compression) if the intraspinal pressure was increased either spontaneously or mechanically. This clue I would deem a very important one and, in

retrospect, points to the possibility of one of the vascular anomalies such as Dr. Gamez mentioned.

Another point worthy of note is the question of spinal fluid block as determined by the hydrodynamics. Ferris and co-workers[2] have shown that, using an effective neck cuff with adequate compression, there probably is no such thing as a partial block. They felt that the question of block was an all or none phenomenon, that either there is or is not a block. They showed quite definitely that as long as there was residual space in the subarachnoid area the size of a lumbar puncture needle, the hydrodynamics would be normal. We are all aware of large intramedullarly tumors which will prohibit the passage of an opaque medium such as Pantopaque and yet have normal dynamics. This, I believe, is of importance. If there is evidence of a hydrodynamic block, then the possibility is that there is a complete block of the subarachnoid space, but even this is not entirely so since, as Ferris has shown in individuals with low cerebrospinal fluid pressure, there might be evidence of a "false block." Thus we feel that the only good and reliable evidence for block is stoppage of the opaque medium in the subarachnoid space.

From the protocol it can be surmised that the initial clinical impression was that of a parasagittal lesion. It was for this reason apparently that a pneumoencephalogram was done (figure 1). Furthermore we can find no evidence of any x-rays of the spinal column having been taken, again pointing to the initial lack of suspicion of a spinal lesion. It was not until after the history was reviewed with the patient and a normal pneumoencephalogram obtained that a spinal cord lesion was suspected. By this time the patient had decided that she had had enough and left the hospital on July 15, 1951 to take care of her business affairs. She returned on July 20 and a myelogram was performed on July 21 (figure 2), without first obtaining roentgenograms of the vertebral column.

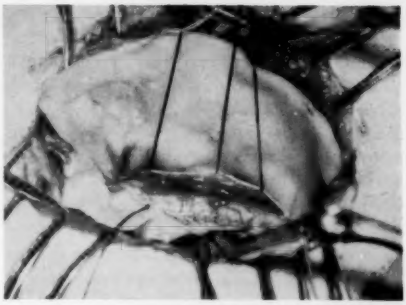

FIG. 3. Appearance of hemangioma at the time of operation on July 23, 1951. The spinous processes and laminae of D11 and 12 and L1 vertebrae have been removed and the dura opened and reflected. The tumor extends from the eleventh dorsal through the first lumbar vertebrae.

Myelography was then carried out, with 3 cc. of Pantopaque injected into the L3-4 interspace. The report:

DR. GERALD M. PETERSON (radiologist): Myelographic study of the lower thoracic and lumbar portions of the spinal canal showed that the Pantopaque moved freely upward, when the patient's head was lowered, until it reached the interspace between the twelfth thoracic and first lumbar vertebra. Here the opaque column divided, and by the time it had reached the upper margin of the body of the twelfth thoracic vertebra, the column had thinned out laterally. The bulk of the material was held below the body of the twelfth thoracic vertebra, but a small amount escaped on either side of the spinal cord extending upward to the level of the body of the tenth thoracic vertebra. The division of the opaque column is evidently due to the presence of the spinal cord, which was apparently considerably larger than is true of the average patient. The appearance suggests the presence of some sort of expanding lesion within the lower portion of the spinal cord. It is possible that arachnoiditis at this level would account for the behavior and distribution of the Pantopaque but I believe that, in all probability, the spinal cord is en-

larged. This is further suggested by the presence of a very large vascular marking in the opaque material just beneath the main shadow produced by the spinal cord. This suggests that there is probably an enlarged vein in this region. It is worthy of note that the vertebrae at this level appear normal in density and there is no narrowing of the intervertebral disk spaces. It is possible, but unlikely, that a herniation of the nucleus pulposis might cause pressure against the cord and produce such changes as noted.

On July 23, 1951 the patient was taken to the operating room and a laminectomy was performed by Dr. Ludwig H. Segerberg. The spinous processes and laminae of the eleventh and twelfth dorsal and first lumbar vertebrae were then removed. The dura was opened and revealed a hemangioma extending from the eleventh dorsal through the first lumbar region (figure 3). The dura was then left opened, the wound was closed, and the patient was returned to the ward in good condition.

The postoperative course was uneventful. The patient has been followed periodically since then. The paraparesis has become slowly but progressively worse. However, she is still able to get along with canes. There have been no other changes in her neurologic picture.

FINAL DIAGNOSIS: Hemangioma T11 through L1.

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■ In 1839, Magendie made a step forward, and discovered a very important fact, which has removed the objection against Sir Charles Bell's theory as regards the anterior roots of the spinal nerves. He found that these roots really cause pain when they are irritated, but that if they are divided, the distal end alone may give pain. He ascertained also that if the posterior roots of any of the spinal nerves are divided, the irritation of the anterior roots of the same nerve no longer causes pain. He concludes, from these facts and some others, that there is what he calls, erroneously, a *recurring* sensibility, which, on the irritation of the anterior roots, manifests itself in this way: The nervous irritation which causes the pain goes, at first, from the parts of the anterior roots in which it has begun, toward the trunk of the nerve, in which it goes to the periphery of the body, and then comes back toward the spinal cord, which it reaches in being conveyed by the ganglion and the posterior roots; so that the current which proceeds from the cord along the anterior roots returns toward it and into it along the posterior ones. We must say that the name of *recurrent* sensibility is a very bad one, because sensibility is a vital property which cannot move from a place toward any other, and therefore cannot be *recurring*. It is the cause, whatever it may be, of the painful sensation, which is *recurring*, and not sensibility.

C. E. Brown-Sequard in *Lectures on the Physiology and Pathology of the Central Nervous System*, published in 1860.

CASE REPORT

Cerebral Metastases from a Mixed Tumor of the Parotid Gland

Sidney W. Gross, M.D. and Arnold P. Friedman, M.D.

THOUGH the literature concerning cerebral metastases from malignant tumors arising in various organs and tissues is extensive, there is still a considerable difference of opinion concerning the management of patients with metastatic brain disease. In a recent review based on extensive experience, Störtebecker[1] presented a follow-up study of 158 surgical cases from Olivecrona's clinic in Stockholm, and advocated an aggressive attitude. In this series of verified intracranial metastatic tumors, enucleable masses were found in 94 cases and solitary masses in 67. The average period of survival following removal of a metastatic brain tumor was 10.5 months, with one patient still living 17 years after operation for a cerebellar metastasis from a hypernephroma.

Our own experience, though based on fewer cases, more or less confirms Störtebecker's conclusions. The purpose of the present report is to record metastases from a rare source—a mixed tumor of the parotid gland—and to pose the question of multiple cranial operations in selective cases.

CASE REPORT

A married white woman of 41 had always been in good health until a mixed tumor of the left parotid gland was removed one year prior to her admission to the Montefiore Hospital. She was symptom-free for about 11 months following the operation, when she began to complain of severe headache which often awakened her from sound sleep. The pain started in the occipital region, radiating forward to the face and involving either the right or left side and sometimes the whole head. The headaches were deep and aching in character, frequently aggravated by turning of the head and neck in the lateral direction and sometimes associated with nausea and vomiting. The patient was given numerous medicaments including analgesics, sedatives, vasoconstrictors, and dilators without any effect. Her past history indicated that she had many emotional problems and her headaches were diagnosed by previous observers as emotional in origin. Her mother had died of a malignancy two years previously, and one year later her brother was diagnosed as having Hodgkin's disease.

On examination the patient showed a slight fuzziness of the optic fundi with fullness of the retinal veins, and showed a tendency to fall to the right. Further studies were suggested but the patient went to another physician, finally returning three weeks later with a complaint of constant severe headaches, fatigue and drowsiness, and diplopia with upward and right lateral gaze. On examination the patient was noted to be drowsy; bilateral papilledema, nystagmus on left lateral gaze, and ataxia of all extremities were noted. Visual field studies disclosed enlarged blind spots. The electroencephalogram showed slow activity in the right anterior frontal region and depression with relatively slow potentials in the left occipital re-

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Read by title at the sixth annual meeting of the American Academy of Neurology, Washington, D. C., April 28–May 1, 1954.

gion. The x-rays of the skull showed erosion of the posterior clinoids and the dorsum sellae.

The clinical impression favored a left cerebellar neoplasm, possibly a metastasis from the parotid tumor. A ventriculogram showed displacement of the ventricular system to the left and depression of the right frontal horn. A right frontal craniotomy was done and a subcortical tumor about 2.5 cm. in diameter was removed from the posterior portion of the superior and middle frontal convolutions. The tumor was well encapsulated and it shelled out without difficulty. Following the operation the patient was free of headache for a time; a left hemiparesis cleared up in ten days. Microscopic examination of the tumor removed from the right frontal region showed it to be similar in all respects to the mixed tumor removed from the left parotid gland one year previously (figure 1).

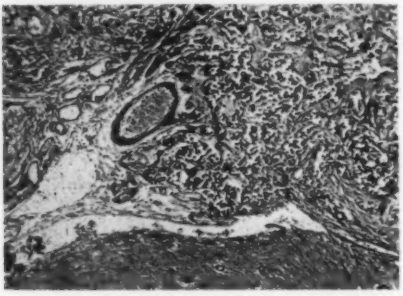

FIG. 1. Photomicrograph of cerebral metastasis. Hematoxylin and eosin stain.

Following a brief period of well-being, the patient's condition slowly deteriorated. Further surgical intervention was deemed inadvisable because it was felt that multiple metastatic lesions were present. The patient expired April 23, 1953, about ten weeks after the craniotomy.

The postmortem examination showed no evidence of recurrent tumor in the left parotid region. The brain weighed 1,410 gm. There was a firm nodule 3 cm. in diameter on the anterior surface of the left cerebellar hemisphere. No evidence of recurrent tumor at the operative site in the right frontal area was found. The lateral and third ventricles were dilated and the aqueduct was three times its normal diameter. The upper part of the fourth ventricle was displaced to the right. On microscopic examination, the operative site was free of tumor. The nodule removed from the left cerebellar hemisphere at post mortem had the same histologic characteristics as the parotid tumor and the right frontal tumor. There were acini and sheets of cells lobulated by connective tissue and foci of tissue suggesting cartilage. No other metastatic tumors were found in the brain or in any other part of the body. The general postmortem examination was not remarkable.

COMMENT

The literature discloses only a few cases of cerebral metastases from a parotid tumor. There were none in Störtebecker's[1] series. Knights[2] found 102 metastatic brain tumors over a period of 26 years at the Henry Ford Hospital. The parotid gland was not the primary site in any case in his series. Ewing,[3] Anderson,[4] Willis,[5] and MacCallum[6] made no mention of cerebral spread from a mixed tumor of the parotid gland. Berglund and Raaf[7] found 36 metastatic tumors in 494 patients with verified intracranial tumors; the parotid gland was the primary site in one. Globus and Metzer,[8] Hare and Schwarz,[9] and Globus and Selinsky[10] reported series of cases of metastatic cerebral tumors with no primary parotid tumor in any of them. It would appear then, though no organ or tissue is exempt,[11] cerebral metastases are extremely rare from mixed tumors of the parotid gland.

In this case, the spread to the brain was by way of the blood stream. There was no evidence at autopsy of erosion of the skull or of involvement of lymph channels.

The treatment of patients with cerebral metastases must be individualized. In the presence of multiple metastases to the lungs, skin, bones, and other organs or tissues, surgical intervention is usually not indicated. However, even in such cases, decompression may be justified for the relief of headache not otherwise controlled. Or, the tumor may be of relatively low-grade malignancy and the removal of a cerebral metastasis in such a case may prolong life in comfort for several months or years. In other cases, admittedly rare, a solitary cerebral metastasis may be the only spread from a removable primary malignant

tumor. In this patient there were only two metastases from a mixed tumor of the parotid gland; the parotid tumor had been completely excised. There was no evidence of recurrence of tumor at autopsy about 16 months later. Of the two cerebral metastases, one was completely removed at operation. Because the patient regressed after a short period of postoperative improvement, it was believed that multiple metastases were present, but at autopsy only a single nodule was found in the left cerebellar hemisphere. Needless to say, had there been any suspicion that only a single lesion remained, attempts would have been made to remove it.

CONCLUSION

In the future a more aggressive attitude will be taken in patients with metastatic brain disease who show no evidence of widespread metastases to the lungs, bones, skin, or lymph nodes. If symptoms recur or do not improve after the removal of one cerebral metastasis, a search should be made for other metastatic lesions. Bilateral carotid angiography, ventriculography, and, if neurologic signs warrant it, exploration are indicated. Admittedly, not many patients will be saved, but in dealing with malignant tumors the stakes are high and heroic measures are justified.

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■ As regards the spinal cord, when we began our researches, the most positive facts among those that were known, seemed to be quite in opposition to the great view of Sir Charles Bell, as they seemed to show that the same part of the spinal cord is employed both in voluntary movements and in sensations. I have tried to show that the same conductors cannot be the agents for both voluntary movements and sensations, inasmuch as those for sensations make their decussation in the spinal cord, while those for motion decussate in the medulla oblongata. In this respect, then, instead of being in opposition to the great principle, to the demonstration of which Sir Charles had employed his whole life, I have brought a striking fact of the truth of this principle. But I repeat that, as regards the channels of conveyance of the sensitive impressions and the orders of the will in the spinal cord, Sir Charles has been completely mistaken.

C. E. Brown-Sequard in *Lectures on the Physiology and Pathology of the Central Nervous System*, published in 1860.

CASE REPORT

Mycotic Meningitis Due to Candida Albicans

A Four Year Recovery

Jacob M. Fine, M.D., Donald A. Franklin, M.D. and Alan S. Lieberthal, M.D.

SEVEN CASES of meningitis due to *Candida* (Monilia) *albicans* have been reported in the literature, the first in 1933 by Smith and Sano.[1] They have all been fatal except one cited by Zimmerman, Frutchey, and Gibbes in 1947 which had been followed for only five months. Our report, a survival of monilial meningitis for four years, is of primary interest because it represents the longest period of recovery to date.[2]

CASE REPORT

A 62 year old white male factory worker first entered the hospital on May 18, 1946 with complaints of weakness, fever, chills, hiccups, dizziness, and diplopia for several days. There was no difficulty in walking, and no paresthesias, anesthesias, tinnitus, or vertigo. His wife stated that he had been confused at times. Systemic review was essentially negative as were the past medical, social, and family histories.

Physical examination showed a poorly nourished, well developed, white male who exhibited frequent violent singultus. The temperature was 101.4°, pulse 76, and respiratory rate 20. The left pupil was larger than the right, and both reacted to light and accommodation, though rather sluggishly. There was distinct nystagmus to the right, left, and upward gazes, with a questionable ptosis of the left lid. The left optic disk was hazy.

Heart and lung examinations were normal. The blood pressure was 110/70. The abdomen was distended. Neurologic examination showed an absent gag reflex, diminished knee jerks bilaterally, and absent abdominal and cremasteric reflexes. There was no nuchal rigidity. The toe signs were not abnormal.

The admission hemogram was unremarkable except for a leukocytosis of 14,450, with 34 per cent nonsegmented polymorphonuclear leukocytes, the total neutrophils being 83 per cent. Toxic granulation was also present. Blood chemistry was within normal limits and blood cultures were negative on two occasions.

A spinal tap performed on the second hospital day showed clear fluid with normal dynamics, chemistry within normal limits, and two white blood cells per cubic millimeter. No smear or culture was ordered at this time.

There was a febrile response of 101 to 102° which persisted from the day of admission. The symptomatology and the clinical course pointed to the possibility of a brain abscess. The patient was placed on penicillin therapy, 40,000 units every three hours, on the third hospital day.

On the seventh day a second lumbar puncture revealed cloudy spinal fluid which, on smear and culture, showed yeast-like budding organisms identified as *Candida albicans*. Since a small pellicle formed on the specimen, a search was made for acid-fast organisms but

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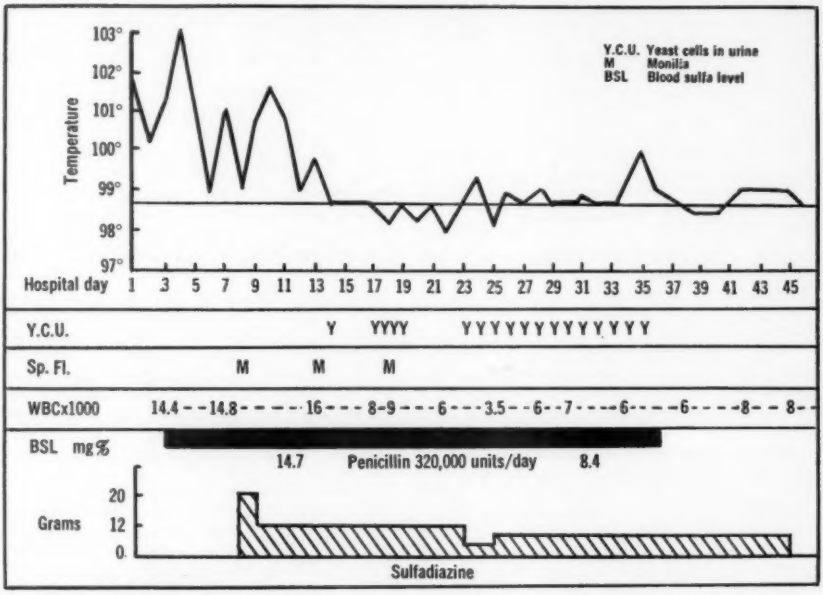

FIG. 1. Laboratory findings in a patient with mycotic meningitis treated with penicillin and sulfadiazine.

none was found. The cells in the spinal fluid numbered 1,800 per cubic millimeter, polymorphonuclear leukocytes predominating. The total protein was 72 mg. per cent. Spinal fluid pressure was normal.

Since the patient had not improved with penicillin, sulfadiazine therapy was begun on the eighth hospital day starting with 8 gm. in two doses four hours apart, and then a maintenance dose of 2 gm. every four hours. Within 48 hours the fever had dropped to 99.8° and then to normal (figure 1).

On the twelfth hospital day a repeat spinal fluid examination showed crystal clear fluid under a pressure of 230 mm. of water. Yeast bodies from the culture of this spinal fluid were again identified as *Candida albicans*. The cells in this tap numbered 1,900, 60 per cent of the cells being neutrophils and 40 per cent lymphocytes.

Stereoscopic skull roentgenograms at this time were negative except for a periapical abscess about one of the lower molar teeth. A culture from this abscess was negative for pathogenic fungi.

As may be seen in figure 1, yeast cells were found in the patient's urine almost daily for about the first month. On the eighteenth hospital day yeast cells were again found in the spinal fluid. At this time the spinal fluid pressure had fallen to 177 mm. of water.

The blood sulfadiazine levels as well as dosage are also illustrated.

White cells in subsequent spinal fluid examinations ranged from 66 to 200 per cubic millimeter, most of which were neutrophils. Three spinal fluid examinations were negative for yeast and bacteria before discharge from the hospital on the forty-sixth hospital day, at which time the patient was ambulatory and the only neurologic residual was slight difficulty in upward gaze. The patient was able to return to work and lead the same kind of life as before his illness.

The second admission was four years later on June 12, 1950. The chief complaint was again that of weakness. The patient had such markedly slurred speech and was so lethargic that the history had to be taken from his wife. She stated that there was a sudden onset of excruciating frontal headaches associated with nausea and emesis two days before admission. Frequent dozing and a tendency to fall to one side or the other on rising was also noted.

There was urinary incontinence and frequency.

Physical examination showed the temperature, pulse, and respirations to be normal, with a blood pressure of 228/116. Grade 2 Keith-Wagener changes of the fundi were seen. There was rigidity of the arms especially. A moderate ataxia, particularly towards the left, was present, as was slight nuchal rigidity. The Kernig and Brudzinski signs were negative. Small muscle atrophy was noted in the hands. There was difficulty in phonation and deglutition. On the right there was a suggestion of hyperreflexia with absent abdominal reflexes, and the Babinski on the right was equivocal. The Babinski and confirmatives were persent on the left. The remainder of the physical examination was normal.

An electroencephalogram was not remarkable. Spinal taps showed xanthochromic fluid and a total protein elevation ranging from 58.8 to 69 mg. per cent, under no increased pressure. After failure of response of the left Queckenstedt, search for the block led to a left carotid angiogram which revealed normal cerebral vessels. At no time during this second admission were any bacteria or fungi isolated from the spinal fluid.

Clinically, the patient became stuporous and exhibited marked nuchal rigidity. A ventriculogram performed on the sixteenth day of the second hospital stay revealed a generalized dilatation of the lateral and third ventricles as well as the visualized portion of the aqueduct of Sylvius. Following this procedure the patient became alert, oriented, rational, and continent. Two days later a communication test, consisting of the injection of phenolsulfonphthalein into the left lateral ventricle, showed that a block was present since none of the dye was recovered in the spinal fluid or urine. Treatment also consisted of fortified penicillin, Telserol, and vitamin B complex. The patient was able to sit in a chair and walk to the bathroom before being discharged.

The last admission on August 6, 1950 revealed that the patient had soon been confined to bed following release from the hospital and had developed chronic constipation, urinary incontinence, and an increasingly high-pitched voice.

The general appearance at this last admission was that of a confused, disoriented, poorly nourished white male. The blood pressure was 166/76. There were absent superficial reflexes. A stiff neck, positive Kernig and Brudzinski signs, generalized incoordination, and coarse horizontal nystagmus were present. Spinal tap was not remarkable.

The blood pressure during this hospital stay rose to 216/140. The patient began to convulse and secretions in the pharynx had to be removed by suction continually. The patient finally lapsed into coma and expired on August 10, 1950.

The pertinent pathologic findings included the following: Grossly no evidence of meningeal thickening was seen, but there was widening and swelling of the convolutions of the vertex of the brain and increased filling of the venous system. The right cerebellar hemisphere was smaller than the left and had a central cavity containing some blood. This hemorrhage had in turn displaced the right hemisphere to the left, thereby compressing the fourth ventricle. This may have contributed to the dilatation of the lateral and third ventricles. The blood-filled cavity in the right hemisphere was organizing and extended into the left hemisphere. There were scattered petechiae about the basal ganglia. In the cortex of the right cerebral hemisphere was a small area of brown pigmentation which on section seemed to stem from a zone of subcortical necrosis.

Grossly the lungs showed some lobular consolidated areas, the kidneys appeared normal, and the right adrenal presented a completely hemorrhagic infarction similar to that seen in the Waterhouse-Friderichsen syndrome.

Microscopically the right frontal lobe of the brain revealed a large zone of cortical necrosis and edema in which there was a dense collection of old blood pigment (figure 2). There was also evidence of meningeal inflammation with dilatation of the vascular channels, giving rise to a picture of a localized edematous old meningitis. There was generalized edema in the whole right cerebral hemisphere along with vascular congestion. The right cerebellum contained a rather large area of recent hemorrhage causing compression of tissues (figure 3). In the left cerebellum there was evidence of old hemorrhage, liquefaction of the clot surrounded by an inflammatory wall (figure 4), and marked old blood pigmentation. There was also perivascular cuffing of lymphocytes representing an old encephalitis (figure 5).

Microscopy of the kidney showed several double contoured yeast organisms within the capsule of a glomerulus (figure 6), and within one of the renal tubules were similar organisms in the budding state (figure 7).

The lungs presented evidence of severe acute pneumonia but no yeast bodies. The spleen had a small area of old infarction with discoloration and hemosiderin pigmentation. A massive hemorrhagic infarction was seen in the right adrenal. The prostate showed some diffuse suppurative prostatitis with a healed infarction in one area.

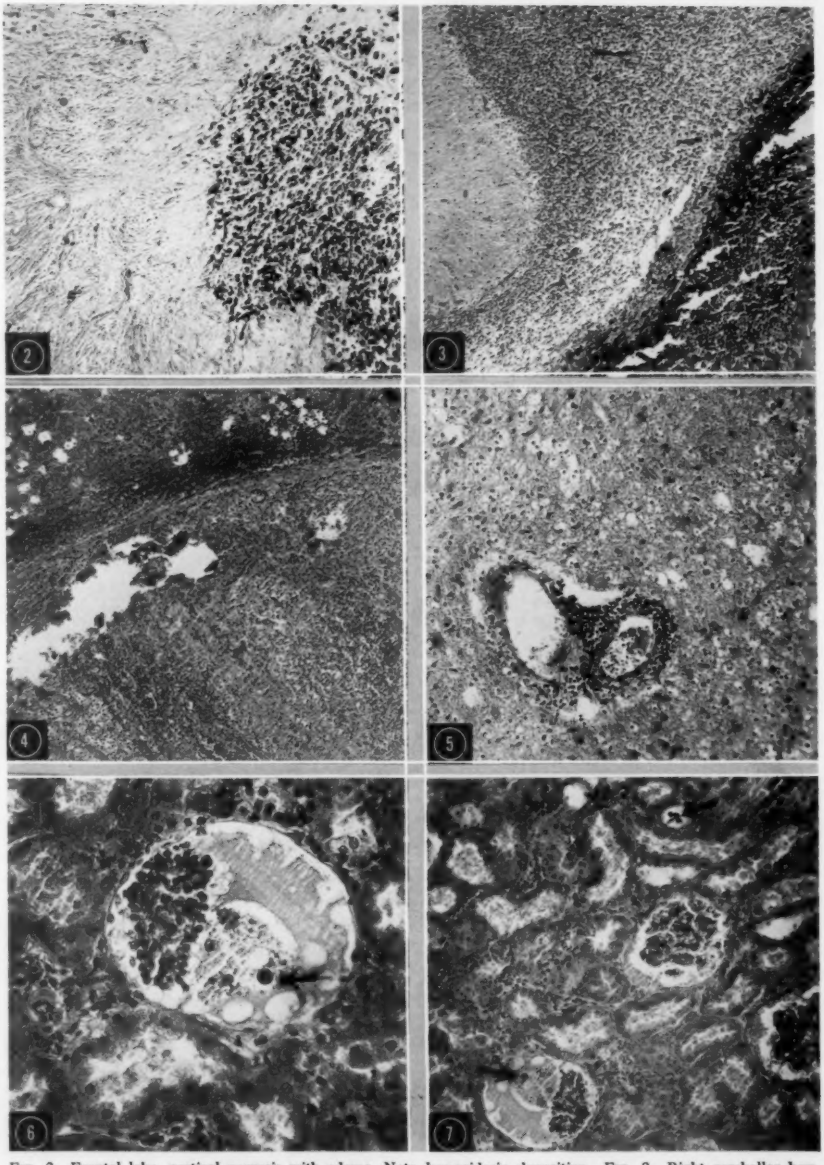

FIG. 2. Frontal lobe, cortical necrosis with edema. Note hemosiderin deposition. FIG. 3. Right cerebellar hemorrhage with compression of contiguous tissues. FIG. 4. Left cerebellum, old hemorrhage undergoing liquefaction, surrounded by inflammatory wall. FIG. 5. Perivascular lymphocytic cuffing. FIG. 6. *Candida albicans* in glomerular capsule. FIG. 7. *Candida albicans* in glomerulus and renal tubules.

DISCUSSION

The findings in this case, both clinical and postmortem, present many interesting features in common with other reported material on monilial meningitis in humans and in experimental animals. For example, a case of monilemia was reported in which there were many hemorrhagic petechiae scattered throughout the brain including the hemispheres, brainstem, and cerebellum along with focal hemorrhages in other organs.[3] There were larger focal hemorrhages in the right cerebellar hemisphere. However, this case showed no lymphoid cuffing and no evidence of cerebral inflammation. The authors concluded that these lesions were due to an acute toxic process and were not embolic or infectious.

Another case showed an internal hydrocephalus, as did our case, along with perivascular round cell infiltration in the brain.[4] This case had at first been diagnosed as a tumor of the third ventricle and the patient died in spite of sulfadiazine therapy and x-ray therapy to the head.

Autopsy of the case of Halpert and Wilkins, which presented many clinical features similar to ours, showed an internal hydrocephalus.[5] There was also thick, creamy liquid in the cisternal spaces and tubercles consisting of central necrosis and giant cells with many septate mycelia in the meninges. The underlying brain tissue was uninvolved. Since the diagnosis had been unsuspected, there was no culture of the spinal fluid. Our case, after recovery of four years, was not expected to show these findings of the acute phase.

Smith and Sano, who reported the first case of central nervous system moniliasis, innoculated rabbits with the strain isolated from their case and one rabbit developed a block of the aqueduct of Sylvius due to edema and congestion, which in turn led to a marked internal hydrocephalus.[1] Cerebral petechial hemorrhages were also seen.

In a case of mycotic endocarditis there was a hemorrhagic area in the brain, as well as areas of perivascular infiltration by lymphocytes, plasma cells, and a few macrophages.[6] Yeast cells were seen in the urine of this patient who expired in spite of sulfathiazole and iodine therapy.

Another case of mycotic endocarditis and meningitis expired after sulfadiazine and penicillin therapy.[7]

Also of interest are the rather variable findings encountered in the spinal fluids of these reported cases, the number of cells varying from 10 to 1,900 and the predominating type of cell also differing from case to case. In addition there is a definite tendency for the chlorides to be lowered in these cases. The chloride levels varied from 585 to 650 mg. per cent. The significance of this lowered chloride level is not immediately apparent and alerts us to the possible confusion with a tuberculous infection of the meninges.

In the period of supposed good health for four years, the blood pressure rose to a rather high level, followed by changes in the retinal vessels. Whether the progressive inflammatory process in the cerebrum and the meninges contributed to its elevation can only be conjectured. The old and the recent hemorrhages in both cerebellar hemispheres explain the clinical findings on the second and final admissions.

An interesting feature is the finding of the *Candida* in both the glomerules and the tubules of the kidney. One can speculate as to its inception, length of abode, and its pathogenicity.

Rabbits, being susceptible to infections of *Candida albicans* when injected intravenously with saline suspensions, die in four to five days with typical abscesses of the kidneys.[8]

Obviously one cannot testify to the efficacy of any therapeutic regimen from one case, but it may be of interest to compare therapy in our case with the only other case of recovery from monilial meningitis, the conclusion in the latter being that streptomycin therapy may have been of value.[2]

Streptomycin had been obtained for our case but, since this was during the infancy of streptomycin antibiosis and since our patient was doing so well on sulfadiazine and penicillin, it was withheld. Penicillin was continued in combination with sulfadiazine because the patient was responding satisfactorily, even though it is well known that penicillin has no inhibitory effect on *Candida albicans* in vitro. In the other reported case of recovery,[2] sulfadiazine was also used but in smaller quantities (2 gm. initially and 1 gm. every six hours) and the authors felt that the sulfonamide did not in any way modify the course of the disease. In our case the maximum of sulfadiazine was employed, along with heavy alkalinization. Supportive parenteral fluids and vitamins were also used as were blood transfusions at intervals of six to seven days. At one time the white blood count fell to 3,500 so that sulfadiazine was discontinued for two days and then started again. A factor in our patient's improvement was his complete cooperation and his ability to tolerate the very large doses of sulfadiazine.

CONCLUSION

This case represents the longest period of survival of a monilial meningitis, the one other survival having been followed for only five months. It is not possible to draw any definite conclusions concerning the efficacy of the therapeutic regimen employed in this single case, but the response to sulfadiazine in maximum dosage was apparently significant. The pathologic findings did not indicate any active foci of meningeal moniliasis, as would be expected in a case recovered from the acute infection for a period of four years, but the necropsy findings closely resembled those reported by other investigators in case reports and animal studies.

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■ In 1851 and 1853, Mr. Lockhart Clarke published his important papers "On the Structure of the Spinal Cord," in which he clearly showed, as Stilling and others had already done, that the posterior roots of nerves are in continuation with the gray matter, and not with the posterior columns; and he tried to show – as had been already done by Sir Charles Bell and Dr. Todd – that the posterior columns, being united with the cerebellum, could not be considered as the only conductors of the sensitive impressions.

C. E. Brown-Sequard in *Lectures on the Physiology and Pathology of the Central Nervous System*, published in 1860.

CASE REPORT

Progressive Facial Hemiatrophy

Erwin M. Jacobs, M.D.

SEVERAL cases of progressive facial hemiatrophy (Romberg's disease) have been reported each year since Archambault and Fromm, in 1931, reported a comprehensive review of the literature including approximately 400 cases recorded previously.[1]

Characteristically, progressive facial hemiatrophy begins in the first or second decade of life but may occur at any age. There is an equal sex distribution. Atrophy may be noted to start any place in the innervation of the trigeminal nerve and may involve not only the subcutaneous and connective tissue but also the cartilages of the nose and ears. Growth of the facial bones is unequal when the onset is in early childhood. As far as can be determined, the muscles are intact. Usually, just one side of the face is involved, with no progression beyond the distribution of the fifth cranial nerve; the atrophy in some cases, however, has extended to the neck and has included one half of the body. The first sign of the disease may be loss of hair about the eyes and on the scalp. Because patches of scleroderma often occur, the two diseases have frequently been linked. Neuralgic pains of the face are commonly present, occasionally even preceding the atrophy. The masticatory muscles are likely to have spasms and trismus for brief periods. Sweating over the involved area and the presence of a Horner's syndrome is variable.[1–4]

Many etiologies have been considered, among which are birth trauma, local trauma, dental infections, and a relationship to scleroderma, epilepsy, or migraine. None of these, however, fits the majority of cases. The pathogenesis also is still unknown, but the relationship to scleroderma, endocrine changes such as a lipodystrophy, parasympathetic disorder via fibers in the trigeminal nerve, and a cervical sympathetic lesion has been postulated. Only the last theory appears to account for the clinical entity most often seen.[1]

CASE REPORT

A 20 year old seaman was admitted to the hospital on April 6, 1954. His chief complaint was the loss of substance from the left side of his face over a period of six months. His first symptom was that of chewing difficulty because his jaw would "lock and hurt deep in the left side." Shortly after this he noted atrophy of the face, beginning in the region of the left malar eminence and progressing to the temporal fossa and cheek. A furrow appeared on the left side of the forehead, and the eyelashes gradually disappeared. He also complained of a drawing sensation and dryness of the left side of the face. The family and past history were noncontributory except for an accidental injury to the left side of the face by a gun butt one and one-half years prior to the onset of his present illness.

On admission to the hospital, the only positive findings were in the examination of the face. There was an obvious asymmetry with loss of tissue on the left side, most marked in

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FIG. 1. Asymmetry and loss of tissue on left side of face. The vertical furrow in the forehead is not seen as clearly in the photograph.

the perioral and malar areas, temporal fossa, and forehead where a vertical furrow was present (figure 1). The distal portion of the nose was also slightly atrophic but the dry, wrinkled appearance of the skin was most marked about the mouth. The hair was sparse in the left eyebrow and eyelashes. The eyelids were slightly reddened. There was no evidence of fifth nerve involvement in the motor or sensory component. No Horner's syndrome, scleroderma, or sweating change was present.

Laboratory studies, including a complete blood count, urinalysis, blood and spinal fluid serologies, blood calcium, phosphorus, glucose, and spinal fluid cell count and protein were all normal. X-rays of the skull, chest, mastoids, facial bones, petrous ridges, and zygomatic arches were normal. An electromyogram showed no involvement of the left masseter, temporalis, or orbicularis oris muscles.

The patient was seen by a dermatologist who found no evidence of scleroderma. The dental staff noted the advanced atrophy of tissue about the caninus, zygomaticus, and quadratus labii superioris muscles, but could not determine any etiologic factor. Daily faradic stimulation for one month produced no improvement. The patient was then given a two-week course of oral cortisone with a maintenance dose of 100 mg. per day. This caused a definite increase of the neuralgic pains and the spasms of the masticatory muscles. A course of glycine (1 oz.) and ephedrine (24 mg.), prostigmine (15 mg.), and stellate blocks was then begun. The drugs were given three times a day and the blocks were done first at weekly intervals and later three times a week. After one month of this regimen, the patient did not complain of pain or trismus. During the second month of treatment he felt there was a slight but definite filling out of the atrophic areas. At this point all of the above medications were stopped and Etamon chloride (800 mg.) was given intramuscularly three times a day for three weeks. On this drug there was no change in his condition.

At the time of his discharge on September 8, 1954, the patient had no complaints and provision was made for receiving further medication at his duty station, if indicated.

COMMENT

In the past, the injection of paraffin subcutaneously, plastic operations, or excision of the cervical sympathetic chain has been recommended to treat progressive facial hemiatrophy.[1,2,5,6] Earlier reports failed to stress drug therapy and it was felt that various regimens could be investigated. Electrical stimulation is often used to treat disorders of the muscular innervation of the face (for example, Bell's palsy) and the failure of the patient to improve with this alone is compatible with the normal electromyogram. Cortisone was administered because of the widespread use of the drug in the collagenous and neurologic diseases of obscure origin. This patient, however, felt worse while receiving the drug. A course of acetylcholine was recommended,[3] but because of the transient action at the myoneural junction, prostigmine was substituted. Glycine and ephedrine were given empirically as an adjunct to treatment, as in muscular dystrophies. The value of the stellate blocks is doubtful since they were given at weekly intervals while the patient was improving, and he noted no further improvement following them. Since a pharmacologic block of the sympathetic ganglia seemed advisable, all other medication was discontinued and Etamon was administered, with no remarkable change resulting.

CONCLUSIONS

1. A case of progressive facial hemiatrophy treated with various drugs is presented.

2. Electrical stimulation was of no value, and cortisone made the patient worse. A combination of prostigmine, glycine, and ephedrine produced slight improvement, while Etamon and stellate blocks did not affect the course of the disease.

3. The possibility exists that the patient was undergoing a spontaneous remission at the time of his discharge from the hospital, but it was recommended in his health record that the status of his illness should be observed periodically.

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■ The great discovery of Sir Charles Bell gives a good instance of the importance of making use comparatively of clinical observation and vivisections. In fact, had Sir Charles had recourse to experiments upon living animals, he probably would have succeeded, at once, in proving the correctness of his theory concerning the roots of the spinal nerves.

Before him, already, many physiologists had, more or less distinctly, foreseen that the nervous conductors for voluntary movements and those for sensation form two distinct sets of nerves. Galen, Boerhaave, Lamarck, Alex. Walker, and others, had had this idea. To Alex. Walker the credit is due of having first published this opinion, that there is a difference in the functions of the anterior and posterior roots of the spinal nerves, one set being employed for volition and the other for sensation; but he did not try to prove, either by experiments or by pathological facts, the correctness of his views; and, led by erroneous ideas concerning the function of the cerebellum, he imagined that the anterior roots of the spinal nerves are for sensation and the posterior for motion.

C. E. Brown-Sequard in *Lectures on the Physiology and Pathology of the Central Nervous System*, published in 1860.

Neurology

BOOK REVIEWS

Clinical Neurosurgery

Proceedings of the 1953 Congress of Neurological Surgeons. 1955. Baltimore: The Williams & Wilkins Company. 201 pages, $8.00.

THIS small book is a record of the meeting of the Congress of Neurological Surgeons held in the latter part of 1953 in New Orleans. At this meeting Sir Geoffrey Jefferson, dean of English neurosurgeons, was the guest speaker and presented three papers, two of which are included in this book. His third paper in this book was presented elsewhere, but is a welcome addition in lieu of the third presentation in New Orleans. The first paper, entitled "Changing Views on the Integration of the Brain," presents a humanistic viewpoint of the modern concepts of brain function and is an interesting commentary on the views of the neurophysiologist who would have us believe that the brain is simply a gigantic communications system. The second and third papers are well documented studies on two conditions which are not very common. The first, "Trigeminal Neuromas," is an excellent resumé of the present knowledge of these rather rare tumors of the temporal fossa. The third, which concerns involvement of the optic pathways by intracranial aneurysms, is quite pertinent at this time when interest is centered on the surgical treatment of intracranial aneurysms.

These three papers, presented in the inimitable style of Sir Geoffrey Jefferson, are delightful reading, both for the easy style of the author and for the wealth of information which is conveyed. The latter half of the book is the presentation of panel discussions on 1) anatomy and physiology of the frontal lobe, 2) psychosurgery, and 3) electrolytes in neurologic surgery. The format of each of these three panels is quite different, but each discusses some of the more controversial aspects of the subject and brings interesting viewpoints together. There is an adequate index to the book.

One should congratulate the Congress of Neurological Surgeons upon this initial effort to publish their proceedings. They were indeed fortunate to have an outstanding authority and brilliant stylist to present such interesting material. This portion of the book alone is well worth the price of the volume. It is difficult to maintain in a written record some of the spontaneity and personality of the speakers which make panel discussions sparkle and interesting. However, the editorial committee has done a very satisfactory job in this most difficult task. The relative frequency of typographical errors should be eliminated with greater experience.

The future volumes of the Proceedings of the Congress of Neurological Surgeons will be awaited with great interest.

A. E. W.

The Human Brain in Sagittal Section

Marcus Singer, Ph.D., and Paul I. Yakovlev, M.D. 1954. Springfield, Illinois: Charles C Thomas, Publisher. 81 pages. Nonflexible binding, $7.75. Flexible binding, $6.25.

This is a photographic atlas of sections of the adult human brain in the sagittal plane. There is no text, aside from brief introductory statements concerning the material, technic, and general viewpoints. Preparations stained for the demonstration of myelinated fibers are utilized. These are reproduced in their entirety at a slight magnification (1.5 times) and with a higher magnification (2.5 times) for the brainstem. The reader is presented with the entire brain section on the page to the left, and with a convenient enlargement of the brainstem of the same section on the page to the right. The printing is quite satisfactory and permits the use of a hand lens.

One of the pleasures of this book is the opportunity to track down familiar sensory and motor pathways. How many readers of *Neurology* have recently seen the actual entrance of the sensory fibers into the thalamus? Here you have such exciting experiences as watching the medial lemniscus and the spinothalamic tract course through the medulla, pons, and midbrain to their actual termination in the posterior ventral nucleus of the thalamus, or of observing the full sweep of the optic radiation from the lateral geniculate body to the lingual gyrus and the cuneus. The atlas is recommended as a reliable anatomic guide and as a source of wholesome anatomic exercise to all neurologists and neurosurgeons.

A. R. V.

Peripheral Circulation in Man

A Ciba Foundation Symposium, edited by G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch., and Jessie S. Freeman, M.B., B.S., D.P.H. Assisted by Joan Etherington. 1954. Boston: Little, Brown and Company. 219 pages, $6.00.

It is interesting to note that 68 of the 210 pages of this book are devoted to technics of measurement of peripheral circulation. Even in this proportionally large section of the book, not all technics which have been proposed are discussed in detail. This demonstrates the difficulty of development of a method for adequate and simple clinical evaluation of peripheral circulation. The discussions, which fortunately have been included, bring out some of the problems not mentioned in the official papers presented at the symposium. Some methods have been worked out very completely on certain aspects of the peripheral circulation (fingertip), while others depend on technics which are more of a laboratory than a routine clinical nature.

There are chapters on neural control of peripheral circulation and some dealing with chemical control. Some very interesting chapters deal with the adaptation to cold and with the problems of vasomotor denervation. The contributors to this symposium came from both sides of the Atlantic; all have made significant contributions to the field of physiology and clinical physiology of peripheral circulation. There are only a few references. This is in keeping with the character of these symposia. They are not meant as an exhaustive review of the field. Rather are they a discussion by a group of experts on the present status of the field, the problems and the directions in which further research should go. The sum total is a small book which nobody interested in this field of physiology will want to miss.

H. D. B.

NEWSLETTER

JUNE 1955

Walter O. Klingman, President
Francis M. Forster, President-Elect
Augustus S. Rose, Vice-President
Thomas W. Farmer, Secretary
Joseph L. Whelan, Treasurer

AMERICAN ACADEMY OF NEUROLOGY

AAN Meeting In Houston Over 400 AAN members, wives, and guests convened in Houston's Shamrock Hotel (April 25-30) for the Academy's seventh annual meeting. Following the customary series of special review courses in neurology, the scientific sessions opened on Wednesday evening (April 27) with a symposium of inquiry into central nervous system vascular disease, and the program continued at a rising pace until the final session on Saturday (April 30).... Between sessions there were pleasant social interludes: cocktail parties, a buffet before an aquacade show featuring the Shamrock Corkettes, and the Academy banquet. Also, for those who had time to spare, convenient arrangements were available to visit the fabulous Texas Medical Center and many other Houston attractions. Congratulations are in order for Program Chairman Francis M. Forster and his committee; Abe Hauser, William S. Fields, and others directing local arrangements; and Mrs. J. C. McKinley, AAN executive secretary.

Cerebral Vascular Symposium Attracts Large Audience Sponsored by the research committee (Augustus S. Rose, chairman), the symposium on "What We Need to Know About Central Nervous System Vascular Disease" proved to be both productive and provocative. Designed to stimulate research interest in this relatively neglected field, the tape recorded discussions were opened by the presentation of a case report illustrating many of the troublesome features in the differential diagnosis and management of cerebral vascular disease. The case report was discussed first by Clark Millikan relative to diagnosis and the need for development of better diagnostic techniques in the light of newer therapeutics. He was followed by Seymour S. Kety with a succinct presentation of what we know and do not know about cerebral blood flow and insufficiency. Next came a presentation by Miller Fisher on related neuropathologic problems, and finally a discussion of hypertension and atherosclerosis by Irvine H. Paige, director of research at the Cleveland Clinic. These presentations and discussions were followed by a lively exchange of questions and views on such controversial subjects as vascular spasm, cerebral vascular insufficiency,

stellate ganglion block, and the therapeutic use of vasodilators and anticoagulants. The proceedings were summarized by Adolph L. Sahs. According to Chairman Augustus S. Rose, "the interest of the tightly packed audience indicates that this type of symposium may become a popular and significant feature of the scientific sessions at future AAN annual meetings."

Fabing Expounds Dimensions of Neurology In an erudite and forthright presidential address, Howard D. Fabing projected the future dimensions of neurology into the unexplored depths of neurochemistry and neuropharmacology.... Tracing the rapid growth of modern neurology since the first meeting of the Academy in 1948, he pointed to the recent advances in neurologic therapeutics and the swing to biochemical research as positive indications of boundless opportunities for the growth of neurology in the years to come. Finally, he described the results of his recent investigations with piperidyl compounds, showing thereby how clinical neurologists associated with chemists and pharmacologists would be well equipped to lead the way in a telling attack on some of the most wretched diseases in man.

Program of Special Courses To Be Enlarged A. B. Baker, chairman of the committee on special courses, announces that the number of special review courses to be given at the 1956 St. Louis meeting will be expanded from six to ten. Tentatively scheduled in the 1956 program are courses in neuropathology (Fae Y. Tichy); neurophysiology (James L. O'Leary); neurochemistry (Maynard M. Cohen); injuries to the nervous system (Gilbert H. Glaser); convulsive disorders (Dave B. Ruskin); clinical electrodiagnosis (EEG & EMG) (V. Richard Zarling); infections of the nervous system (A. L. Sahs); neurologic disorders of infancy and childhood (Preston Robb); current advances in neurology (Joe R. Brown); and a course on common neurologic syndromes for general practitioners (Benjamin Boshes) .... At the Houston meeting, 96 individuals were enrolled in the courses, with the greatest number participating in the course on neuromuscular disorders given by G. Milton Shy.

Logothetis Wins Auxiliary Prize The first annual prize of $100 awarded by the AAN Woman's Auxiliary for the best manuscript on a neurologic topic went to John Logothetis for his essay on proteins of the cerebrospinal fluid. Logothetis (the name means deliverer of a speech), born in Salonika, Greece, is a member of A. B. Baker's resident staff. With a group of young colleagues from Minneapolis, he motored to Houston and presented his prize essay during the scientific sessions. Later, at the banquet he was awarded the prize by President Fabing.

Texas Hospitality to Academy Members Wednesday afternoon (April 27), early arrivals for the AAN meeting agreeably tasted Texas hospitality when over 200 members, guests, and wives joined at a cocktail party sponsored by the Houston-Galveston AAN members at the Doctors' Club.... Following the cocktail party, Dr. and Mrs. Abe Hauser of Houston provided dinner in their attractive home for the group.

Klingman Becomes New AAN President At the close of the Houston meeting, Walter O. Klingman of Charlottesville, Virginia became the new president of the AAN for the period 1955-1957. Other newly elected officers are: Francis M. Forster, president-elect; Augustus S. Rose, vice-president; Thomas W. Farmer, secretary; and Joseph L. Whelan, treasurer. Added to the Board of Trustees were Robert W. Graves, succeeding T. J. C. von Storch, and Richard L. Masland, succeeding Titus H. Harris.

Auxiliary Elects New Officers Newly elected during the executive sessions of the AAN Woman's Auxiliary are: Mrs. Franklin O. Meister, president; Mrs. James Sagebiel, president-elect; Mrs. A. L. Sahs, vice-president; Mrs. Russell N. DeJong, secretary; and Mrs. Dave B. Ruskin, treasurer.

* * * * * *

Symposium Planned for ANA Meeting President Percival Bailey has arranged a symposium on the electrical activity of subcortical centers as a highlight of the eightieth annual meeting of the American Neurological Association, to be held in the Palmer House, Chicago (June 13-15). Named as participants in the symposium are Reginald G. Bickford, Frederic A. Gibbs, Robert G. Heath, Herbert H. Jasper, and E. A. Spiegel. The remainder of the sessions will follow the same pattern as in previous years.... Preceding the ANA meeting, also at the Palmer House, are meetings of the American Association of Neuropathologists, American Electroencephalographic Society, and the Society of Biological Psychiatry. In addition, there will be a symposium on the histo- and cytochemistry of the nervous system under the chairmanship of Heinrich Waelsch of Columbia University.

Additional Societies Join NCRND A. B. Baker, chairman of the National Committee for Research in Neurological Disorders, announces the admission of two aditional national societies to its membership: the National Foundation for Infantile Paralysis and the National Association for Retarded Children. The National Committee now has representation from seven voluntary health organizations interested in neurologic

disorders. Besides the two new members, they are: United Cerebral Palsy, National Multiple Sclerosis Society, National Epilepsy League, Muscular Dystrophy Associations of America, and the National Society for Crippled Children and Adults (see Newsletter, July 1954).... The National Committee continues to devote much of its activities to the encouragement of public support of research in neurologic disorders.

Here and There At the Shamrock, Mr. and Mrs. Paul B. Hoeber gave a cocktail party, Thursday (April 28), for the contributors to Baker's CLINICAL NEUROLOGY.... Dr. Edward F. Domino, assistant professor of pharmacology at the University of Michigan and AAN associate member, has been awarded the Michigan Society of Neurology and Psychiatry Research Award for 1955. This award of $250 is given for original research to graduate scientists during the first five years of their training or experience.... William C. Noshay has been appointed head of neurology at the Henry Ford Hospital, Detroit, succeeding Gerald O. Grain who has relinquished his administrative duties at this hospital.... According to Webb Haymaker, Dr. Tillie Edinger, anthropologist at Harvard, was brought to Frankfurt for the celebration of the Edinger Centenary at the Edinger Institute of the University of Frankfurt (April 15). Among those on the scientific program were Profs. Drs. M. Flesch-Thebesius, A. Lauche, H. Spatz, and W. Krucke.... A recent visitor to the U. S. A. was Dr. Purdon Martin, senior physician at the National Hospital, Queen Square, London.... J. Gordon Millichap, associate professor of pharmacology, University of Utah, and Donald O. Hebb of the Montreal Neurological Institute have come to the National Institute of Neurological Diseases and Blindness as visiting scientists....

Percy Bailey

A NEW EMOTIONAL STABILIZER FOR NEUROPSYCHIATRIC THERAPY

Serpasil, in a recent study,[1] proved to be a valuable supplement in the treatment of neuropsychiatric conditions, including schizophrenia, paranoid and manic states, general paresis with psychosis and some cases of depression. In many instances it eliminated the need for electroshock therapy, restraints, seclusion and barbiturate sedation.

Combative, uncooperative patients in general became friendly, cooperative, cheerful, sociable and more amenable to psychotherapy under Serpasil. Hyperactive patients became sedate, noisy patients quiet, depressed patients alert.

Serpasil produced remissions in 20 of the 74 patients studied. Eight were discharged from the hospital. Long-term effects of treatment have not been determined.

If extended studies confirm preliminary findings, the authors state, Serpasil will be one of the most important therapeutic agents in the history of psychiatry.

Dosage information will be found in a CIBA advertisement elsewhere in this journal.

Parenteral Solution (for psychiatric use only), 2.5 mg. Serpasil per ml., 2-ml. ampuls.
Tablets, 1.0 mg. (scored), 0.25 mg. (scored), 0.1 mg.
Elixir, 0.2 mg. Serpasil per 4-ml. teaspoonful.

1. Noce, R. H., Williams, D. B., and Rapaport, W.: J. A. M. A.: 156:821 (Oct.) 1954.

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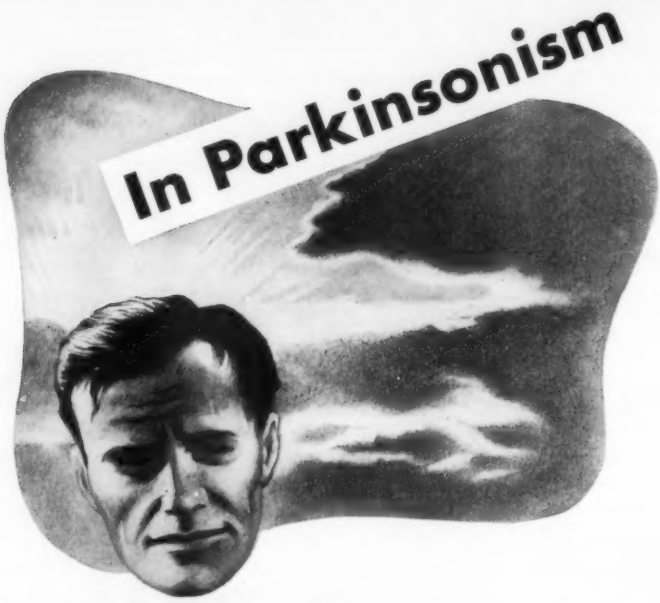

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1. Am. J. Pharm. — 117:319-326, 1945 2. N. Y. State Journal of Medicine 49/1285
3. Conference National Academy of Sciences Sept. 9, 1950

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Romilar hdydrobromide, the first synthetic, non-narcotic drug to have the same antitussive action as codeine without sharing its drawbacks, has been introduced recently by Hoffmann-La Roche Inc., Nutley, New Jersey. This drug represents a significant advance in cough therapy since it has a specific effect in suppressing the cough reflex without causing addiction or constipation. Published statistical analyses of more than 18,000 observations made during clinical comparison of Romilar and codeine have established that 10 mg. of Romilar is equivalent in antitussive activity to 15 mg. of codeine. Unlike codeine, however, Romilar is non-narcotic; it has no analgesic activity, no constipating effect, and no addiction liability.

Chemically, Romilar is a d-3-methoxy-N-methylmorphinan hydrobromide. It is available in double-scored oral 10 mg. tablets as well as in a syrup containing 10 mg./4 cc.

DIBULINE FOR MUSCLE SPASM

Dibuline Sulfate, Merck, 25 mg. per cc. in sterile solution, is a synthetic, antispasmodic agent with a high rate of effectiveness in the management of certain smooth muscle spasm. It exerts both parasympatholytic and direct spasmolytic effects. Dibuline sulfate is exceptionally potent and unusually prompt in its action, usually achieving its full spasmolytic effect within one to ten minutes.

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METHIUM-RESERPINE COMBINATION

The potent hypotensive agent methium chloride has now been made available in combination with the tranquilizing Rauwolfia serpentina derivative, reserpine, in a single tablet for the control of mild to severe hypertension, by Warner-Chilcott Laboratories, New York City, the pharmaceutical division of Warner-Hudnut.

The two drugs have been incorporated into one tablet because of the increased effectiveness of low doses of methium chloride when the drug is combined with low doses of reserpine.

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*Textbook of Pharmacology, (Saunders) 1952.

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TWO SKF ANTICHOLINERGICS

Two dramatic new anticholinergic preparations, each bringing 12-hour relief day or night for sufferers of peptic ulcer, hypersecretion, and spastic conditions of the gastrointestinal tract, come to the medical profession through Smith, Kline & French Laboratories, Philadelphia, Pennsylvania.

Trademarked Prydon Spansule capsules and Prydonnal Spansule capsules, the SKF products represent late additions to the firm's growing line of sustained release medications. Rather than requiring adherence to a rigid t.i.d. or q.i.d. dosage schedule, a single Prydon or Prodonnal Spansule capsule provides an uninterrupted antisecretory and antispasmodic effect that lasts throughout the sleeping hours or over the patient's entire active day.

Through the simultaneous marketing of two very closely related products, the Philadelphia pharmaceutical firm is attempting to meet the specific individualized requirements in treating patients with common cases of peptic ulcer and spastic conditions, as well as patients with more difficult cases. SKF announced that Prydon Spansule capsules are available in two strengths (0.4 mg. and 0.8 mg. belladonna alkaloids), and provide the physician with flexibility in achieving the proper dosage schedule for each individualized case. Prydonnal Spansule capsules, containing 0.4 mg. belladonna alkaloids plus 1 gr. of phenobarbital provide an additional sedative action so often desirable in these cases.

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More potent antianemic therapy in a smaller, easier-to-swallow tablet is provided by the new Iberol Filmtab introduced by Abbott Laboratories, North Chicago, Illinois. Thanks to Iberol's strengthened therapeutic formula, daily iron and nutritional requirements are obtained from two instead of three tablets per day. The new Iberol tablet's film seal completely masks the taste of the ingredients. While the old coated tablet weighed 1.65 gm., the new weighs only .82 gm. and is the smallest hematinic of its kind available. Despite its small size (smaller than a dime), Iberol Filmtab provides therapeutic amounts of the basic antianemia agents, plus essential nutritional factors, including the complete B complex. Two tablets contain, in addition to the B-factors: 210 mg. ferrous sulfate, U.S.P. (the active ingredient for treatment of iron-deficiency anemia); 1 U.S.P. oral unit vitamin B_{12} with intrinsic factor concentrate (the anti-pernicious anemia activity). This potent new formula eliminates the need for additional B-complex supplefentation.

(Continued on page 22A)

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Medical student research fellowships, available to medical schools throughout the United States and Canada, are now being offered for the current year by Lederle Laboratories Division, American Cyanamid Company, Pearl River, New York.

The fellowships, not exceeding $600 for any one individual, are intended to relieve some of the financial burden of students who desire to devote their summer vacations to basic research in the preclinical medical sciences. Selection of students to receive the award will be made by the dean of the medical school or his selection committee. Students who apply must be of good scholastic standing and have the consent of the faculty member under whose supervision their research is to be conducted. Such research may be carried on in another medical school if the arrangements are satisfactory to faculty authorities in both schools.

SHARP & DOHME INTRODUCE SUSPENSION REMANDEN - 100

Suspension Remanden - 100, combining penicillin and Benemid probenecid, the drug which is particularly effective in increasing and prolonging high plasma levels of penicillin, has been released for national distribution by Sharp & Dohme, Division of Merck & Co., Inc., West Point, Pennsylvania. The produce will retain its potency for as long as two years without refrigeration.

Greater confidence may be placed in oral penicillin therapy, since plasma penicillin concentrations are increased by Benemid and demonstrable levels may be maintained for longer periods. The palatability and attractive appearance of Suspension Remanden - 100 make it readily acceptable to infants and children who so frequently object to swallowing tablets or capsules. The necessity of crushing tablets is avoided and more flexible dosage is assured. By providing more effective, more dependable oral penicillin therapy, injections frequently may be eliminated and the painful local reactions sometimes following intramuscular injection can be avoided, a decided advantage in pediatric practice.

LEDERLE ANNOUNCES ANTICHOLINERGIC

Pathilon tridihexethide, a new anticholinergic which gives prompt pain relief from peptic ulcers with a minimum of side reactions, has been announced by Lederle Laboratories Division, American Cyanamid Company, Pearl River, New York. Primarily intended for the medical treatment of ulcer, Pathilon interrupts parasympathetic nerve impulses, thereby relieving gastrointestinal spasms and inhibiting the secretion of irritating gastric juices. The drug has also been found valuable in the treatment of chronic hypertrophic gastritis, intestinal hypermotility, and certain cases of colitis. Clinical tests have shown that dry mouth, visual disturbance, urinary retention, and stoma-

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titis – side effects usually encountered in anticholinergic treatment with other agents – occur less frequently after administration of Pathilon. Pathilon, and Pathilon combined with 15 mg. of phenobarbital, is available in 25 mg. tablets in bottles of 100 and 1,000.

ISOTOPE PRODUCTION AT ABBOTT

Radioactive isotope production is expected to be tripled at the Oak Ridge unit of Abbott Laboratories as a result of a plant expansion now underway. By August work will be finished on an addition which will double the building's floor space and triple its potential capacity.

Radioisotopes originally were undertaken by Abbott back in 1948 as a service to research institutions. Compared with other product groups, radioactive materials still represent a relatively small part of Abbott's pharmaceutical business.

Abbott began its isotope production at the company's research headquarters in North Chicago, Illinois, but moved that operation to Oak Ridge in 1950 so materials from the nuclear reactor could be handled more speedily and without loss of activity through the limited half-life. Some isotope production and most of the research still is done at North Chicago.

Abbott radioisotopes are used for diagnosis and treatment of tumors and other conditions.

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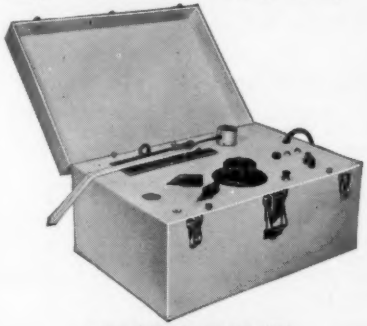

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A simplified inexpensive instrument for recording electrical potentials of the brain. Built-in interference eliminators permit use anywhere. Inkless records — no photography or film development required. Instantaneous localization with any 2 of the 10 leads.

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SERIAL
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Model 110 Universal Automatic Seriograph

Here is automatically controlled serial angiography with highest quality, standard size pictures and standard developing procedures!

Full control by Radiologist permits test pictures and delays during picture cycle. The 12 individual cassettes, each with its own set of screens, give you 11" x 14" (or smaller) standard pictures for adult angiographic studies.

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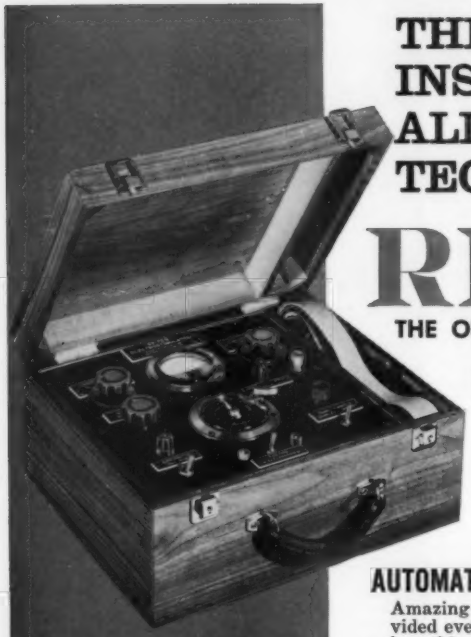
MODEL RC-47C



- CONVULSIVE THERAPY — full range
- FOCAL TREATMENT — unilateral and bilateral convulsions
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FREEDOM FROM SIDE EFFECTS

Model RC-47C provides remarkable freedom from physical thrust, confusion, apnea, memory loss and other side effects.

AUTOMATIC SAFEGUARDS

Amazing reduction of thrust is automatically provided even at full scale current. Patients are often breathing before completion of seizure.

PREFERRED FOR AMBULATORY PRIVATE PRACTICE

During treatment patients do not disturb quiet office atmosphere since confusion and excitements are avoided. These features are equally valuable in hospitals.

VERSATILE — EASY TO OPERATE

The simple controls allow all established techniques. Merely switch to treatment and adjust current with only one control knob.

INCREASED EFFICIENCY OF CURRENTS

Minimal stimulation is required to produce an effective seizure. The use of such biological currents tends to eliminate the undesirable electrical energy component which is the cause of unwanted side effects.

RUGGEDNESS AND ACCURACY

These instruments do not require adjustment for very long periods of time. Yet they are so accurate as to allow for delicate work within the brain.

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Current, improved techniques are based on Model RC-47C and provide the means of treating resistant and difficult cases with therapeutic success.

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without relapse

In post-infection neuritis (following upper respiratory or virus infection), one ampul of Protamide daily for five days has been shown to produce complete recovery without relapse in 85% of patients when treatment was started during the *first week of symptoms.**

You can count on comparable results in your own practice when you

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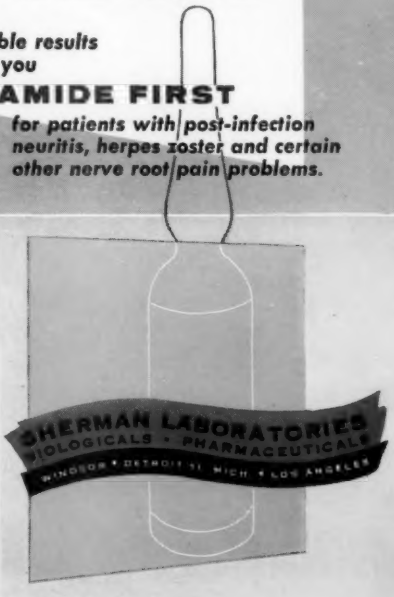
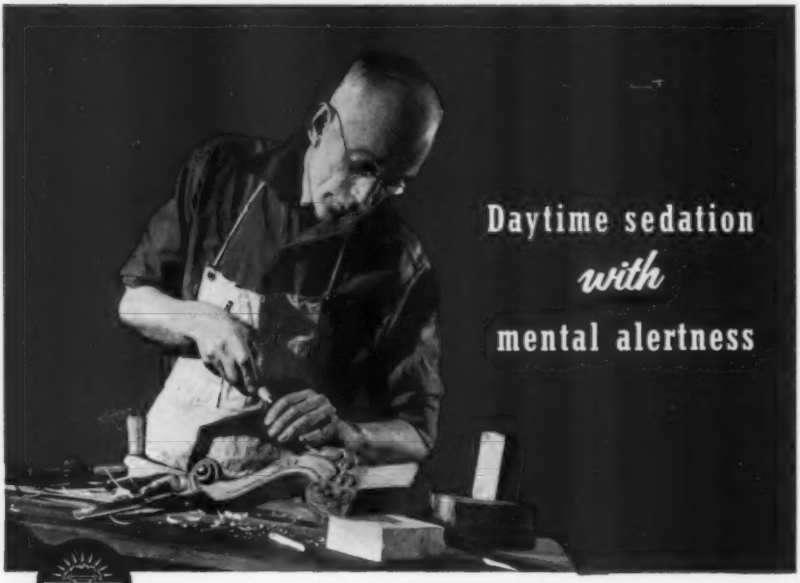
The solution is straw colored with an adjusted pH of 5.9. It is virtually painless on administration and is used intramuscularly only.

Protamide is stable at room temperature and is packaged in 1.3 cc. ampuls in boxes of ten.

*Smith, R. T., New York Med. 8:16, 1952.





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—in depressed and agitated states

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hypertension
hyperthyroidism
convulsive disorders
difficult menopause
hyperhidrosis

Neurotic depression hiding beneath the disguise of multiple physical complaints is an everyday problem in medical practice.

For effective sedation in these cases, and as a means of restoring harmonious relations between patient and environment, Mebaral has been found especially suitable because it lacks excessive hypnotic action.

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Adults—32 mg. to 0.1 Gm. (optimal 50 mg.), 3 or 4 times daily.

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SUPPLIED:

Tablets of 32 mg. (½ grain)
50 mg. (¾ grain)
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